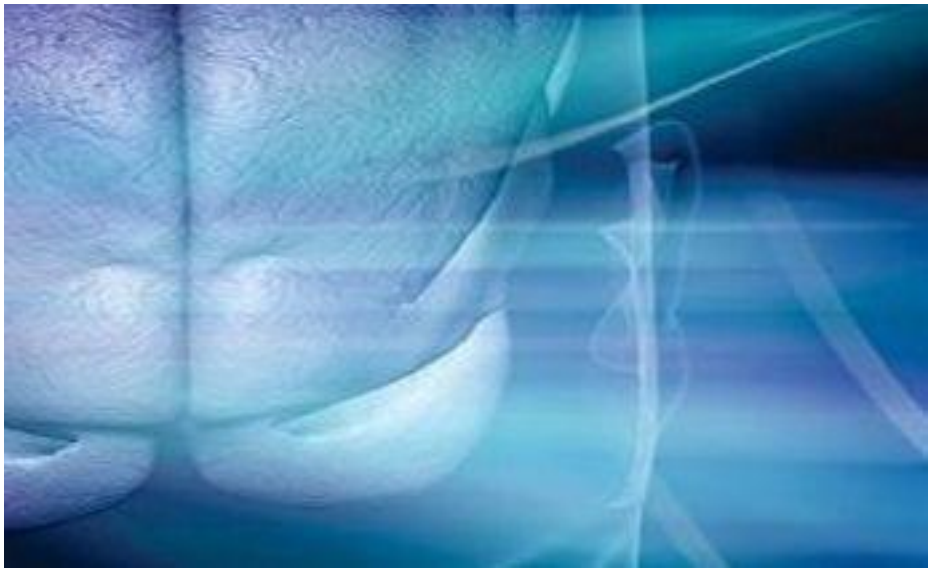

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Papers submitted should be original documentation, including photographs. The papers should be single column, double-spaced. The title should be in title case and bold, followed by Authors, degree, organization and city, state.

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EDITOR'S PAGE

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Welcome to the Journal of the American Organization of Neurological Surgeons and the American College of Osteopathic Surgeons Neurosurgical Section. This volume is composed of the Residents' annual papers that were submitted but not published elsewhere. It is therefore dedicated to the future Neurosurgeons and their education. All papers were reviewed by the peer review committee and selected for awards. The papers submitted are excellent, representing some of our talented colleagues. Issues will be published annually. I hope that this issue will spread the knowledge of our residents and our section. We will continue to solicit annual papers and all papers submitted at the annual meeting. This is your Journal paid for by your annual dues. This issue is available on our website AOANeurosurgery.org. This is your organization; please support it as you can.

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Editor

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1st Place
Scott Glickman, DO
Multimodal Neurocritical Care Monitoring: Conceptual Approach And Indications
Award: $1500

2nd Place
Ripul Panchal, DO
Intraventricular Administration Of Recombinant Tissue Plasminogen Activator To Treat Basal Ganglia Hemorrhage With Intraventricular Extension
Award: $1000

3rd Place
Frank Hux, DO
Purely Endoscopic Versus Traditional Open Microvascular Decompression in the Treatment of Vascular Compression Syndromes
Award: $500

MULTIMODAL NEUROCRITICAL CARE MONITORING: CONCEPTUAL APPROACH AND INDICATIONS

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Keywords: neurocritical care, intracranial pressure, neuromonitoring, technology

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Abstract

The neurologically critically ill patient requires a comprehensive approach to evaluation and management. Standard intensive care monitoring equipment may lead to incorrect assumptions of the underlying pathophysiology at any given time. With the advancement of neurocritical care comes the evolution of advanced neurological monitoring techniques, technologies, and concepts. Much initial knowledge of brain injury was gained via the study of head trauma. More recently, application of the same techniques to other conditions, such as stroke, hemorrhage, and metabolic brain disease has expanded the concepts, goals, and benefits of multimodal neuromonitoring. The current review attempts to summarize and update basic understanding of many of the advanced neuromonitoring tools employed in the neurocritical care unit, from basic assessments of intracranial and cerebral perfusion pressure, to advances in cerebral blood flow determination, cerebral oxygenation and temperature, and brain metabolism with microdialysis, as well as non-invasive assessments of blood flow and electrical activity. Not all neurocritical care illnesses can be approached the same, nor can all patients with similar brain injury be expected to follow the same disease course. Therefore, combination or multimodal neuromonitoring of patients becomes more important to trend different physiologic parameters in each patient as indicators of the underlying and ongoing pathophysiologic mechanisms that will enhance and guide decision making, intervention, and improve outcome.

Introduction

Although detailed multimodality neuromonitoring of the acutely injured brain is not yet performed routinely in most hospitals, it represents a logical way to evaluate, understand, and optimize the neuromedical management of the critically-ill neurologically injured individual. The overall goals are to salvage uninjured tissue and to minimize or prevent ongoing secondary brain injuries. Conceptually, a proactive mind-set to recognize as early as possible the events leading to ongoing secondary brain injury should always take priority over simple reactive approaches after worsening has already occurred. Therefore, knowledge of fundamental physiology and pathophysiologic mechanisms, combined with the tools of the modern neurocritical care armamentarium allow anticipation and proper advanced monitoring to avoid injuries that otherwise go unrecognized until clinical sequelae become pronounced, and often irreversible. As with other intensive care settings, the neuroscience critical care unit requires interplay between abundant patient care systems and monitors, as well as the various systems within the hospital setting itself. Attempts to document, detail, and advance the state of care and continually strive to improve outcomes has led to the development of expanded record keeping, research databases, and quality assessment systems interconnected with the daily activities to best serve patients (Figure 1).

The clinical examination is one of the foundations of clinical neuroscience. However, many patients in the neurocritical care unit (NSICU) are comatose, intubated, sedated, or otherwise not accessible for a detailed examination, and hence, methods were soon adapted to facilitate monitoring of the brain performance. Traditionally, ICP and CPP have been frequently employed to provide a moment-to-moment estimate of the intracranial hemodynamics. However, other major determinants for brain tissue survival such as adequacy of cellular oxygenation, glucose metabolism, and neuronal functioning both at the larger (electrical) and regional (cellular) levels have only been recently been introduced to the NSICU patient's bedside (Figure 2). As these monitoring techniques are now available to provide crucial, real-time information about brain performance an updated review on how and why to measure such parameters seems very timely. He we summarize our own and the literature-reported experience of neuromonitoring in the NSICU. For reasons of succinctness, we are omitting a discussion about modern, minimally-invasive, real-time monitoring of systemic organ performance (i.e.

cardiovascular and hemodynamic and combined neuro-cardiac monitoring) to be reviewed in follow-up.

Goals

The main goal of multimodality neuromonitoring is to optimize the cellular environment of the injured brain region closest to physiological conditions in order to maximize neurological salvage and recovery. It is generally accepted, but not necessarily proven with clinical and scientific veracity that the more complete our understanding of the acute hemodynamic and metabolic dysfunction, the greater the likelihood to recognize ongoing or developing secondary brain injury. Early detection of secondary worsening of neuronal functioning, or more importantly, the proactive anticipation and recognition of physiologic trends known to correlate with development of detrimental deterioration, has become a cornerstone of modern neurocritical care. However, such premise also implies several key issues mandated as understood with respect to proper utilization of advanced neuromonitoring. First, neuromonitoring should ideally be performed within the injury region, i.e., on the side of a large hemispheric infarction, and not at distant, non-affected brain sites as otherwise the obtained measurements do not accurately reflect tissue performance. Second, depending on the predominant primary brain injury mechanism, certain brain performance measurements are more important to monitor than others; hence, a priority list should be established for each individual patient to prioritize the most informative monitoring parameters particular to that patient and to avoid the indiscriminate use of additional or suboptimally selected invasive monitoring. For example, monitoring intracranial pressure (ICP) in patients at risk for the development of secondary brain swelling after completed large ischemic infarction or the occurrence of new mass effects from delayed bleeding complications proves appropriate and effective. In contrast, ICP monitoring will not be of great value in a patient at risk for vasospasm after subarachnoid hemorrhage where regional changes in cerebral blood flow or slowing of electrical activity are more indicative of worsening brain function. Third, once monitoring parameters are obtained, there is the common danger of either discounting or misinterpreting the obtained values. For example, it takes expertise and diligence to understand the role of an abnormal monitoring result. Even simple ICP elevations may either reflect erroneous inclining values in an otherwise asymptomatic patient indicative of baseline drift of an intraparenchymal brain pressure probe, or the elevation may herald dangerous plateau waves in a noncompliant, swollen brain with autoregulatory failure.

Intracranial Pressure (ICP), Cerebral Blood Flow (CBF), and Cerebral Perfusion Pressure (CPP)

As widely known, continuous ICP readings are most commonly obtained from intraventricular and intraparenchymal devices such as external ventricular catheters (EVD), Camino™ or Ventrix™ monitors, and less frequently from subdural or epidural bolts (i.e. Richmond System, etc.). Importantly, intraparenchymal microsensors and strain gauges have a minimal associated risk (i.e. infection, local bleeding), but may experience drift (upward or downward inaccuracy of the zero point) over time, which is not seen with EVD's. Thus, EVD catheters are still considered the gold standard for ICP monitoring. Furthermore, the EVD catheter also allows for therapeutic drainage of CSF that is not an option with standard ICP monitors alone. The monitored ICP waveform already discloses important diagnostic information about the brain compliance; for example, elevation of the second peak (P2 or tidal wave, which is the results of the cardiac dichrotic notch) seen in excess of the first peak (P1 or percussion wave) are considered to be provide valuable information for decreasing brain compliance and increasing risk of brain injury for high ICP's, (Figure 3).[1]

Until recently, continuous, real-time cerebral blood flow (CBF) measurement was not possible at the bedside. Most commonly, xenon-enhanced CT scanning allowed a semi-invasive measurement of CBF at the time point of the examination. While transcranial Doppler ultrasound (TCD) allows a continuous measurement of flow velocity it can only used to approximate the concurrent blood volume flow in the insonated arterial segment. Nowadays, two direct and continuous methods are available to measure CBF. First, laser Doppler flowmetry (LDF) developed in the 1980's functions on similar physical principles as the TCD monitoring, except that the probe is directly inserted through a burr hole into the brain white matter.[2] A monochromatic laser light is emitted measuring both the concentration and velocity of red blood cells to generate a flow signal. Limitations are very small sample volume (~1 mm^3) and the inability to only measure relative flow changes transcribed to the monitor as arbitrary flow units.[3] The second method is based on thermal diffusion which allows a quantitative estimate of regional CBF. Thermal diffusion correlates the dissipation of heat, generated (~39º Celsius) and controlled by a small distal thermistor as it arrives at the second, more proximal thermistor outside of the direct thermal field of the distal heat generator. Based on the tissue's ability to dissipate the heat deriving from the distal thermistor a quantitative estimate of CBF can be

obtained and expressed as mL/100g/min.[4] The clinician can choose CBF monitors from several manufacturers such as Laserflow, Vasamedics Inc, St Paul, MN, USA: OxyFlo, Oxford Optronics, Oxford, UK; Bowman Perfusion Monitor, Ansprach Companies, Gloucester, MA, USA; Saber series, Flowtronics Inc, Phoenix, AZ, USA.

Measuring CBF has been applied to patients with subarachnoid hemorrhage (SAH)[5], head trauma[6], and patients undergoing neurosurgical operations.[7] Under physiological conditions neurons shift from aerobic to anaerobic metabolism as the CBF drops below 18 mL/100g/min.[8] Careful adjustments are required for the increased metabolic demand of injured brain tissues. In addition, CBF measurements are only obtained locally, thereby neglecting the variations in CBF throughout the remaining, non-monitored brain compartments, both injured and uninjured. However, as neurocritical care relies heavily on the principle of blood pressure augmentation in many forms of brain injury (i.e. SAH, vertebrobasilar insufficiency, stroke, revascularization, CPP salvage, etc.), CBF monitoring is certainly a very helpful adjuvant to the clinical management of such patients (Figure 4).[9]

Intracranial pressure (ICP) remains the primary neuromonitoring parameter selection in general, due to the long history and simplicity by which it can now be determined. Further, most neurocritical care physicians and neurosurgeons are quite comfortable discussing ICP in patient care. As a neuromonitoring parameter, it adequately allows for assessment of global pressure, but not local phenomena. A major downfall to it's sole use is that it may remain reasonably normal along an extensive range of values, until a critical point when it becomes difficult to manage (Figure 5). The interplay between cerebral perfusion pressure (CPP) and ICP, the latter delineating the main force counteracting arterial flow and hence arterial perfusion, are the principal determinant of the autoregulatory brain perfusion response (Figure 6). Brain perfusion remains rather constant between mean arterial pressures (MAP) from 80 to 100 mm Hg. Normal ICP ranges from 5 to 10 mmHg resulting in a CPP (MAP-ICP) of approximately 70 to 85 mm Hg. Consistent and continuous MAP measurement should be obtained from intra-arterial catheters. True (regional) CPP measurement may vary as much as 30 mm Hg from the calculated values utilizing the CPP formula when compared to CPP obtained from TCD readings.[10] Of note is that for more accurate CPP estimation the zeroing of the arterial transducer should be done at the level of the foramen of Monroe in order to obtained meaning CPP values. However, to avoid physical inconsistencies in anatomy and height, the most accurate assessment of CPP is made

when the foramen of Monro, heart, and intra-arterial catheter and transducer are all at the same height (i.e. supine position), although this may be at times hazardous to assess, when ICP becomes critically elevated. Autoregulatory failure or the inability for cerebral arteries to regulate and adjust their luminal diameter in response to systemic blood pressure changes, lead to direct dependency of the cerebral perfusion on the CPP (Figure 7). Commonly, a CPP threshold of >60 mm Hg is used clinically to maintain adequate brain perfusion. However, CPP minimum of 60 has been inadequately proven in larger series and may vary significantly between patients and between disease entities and underlying pathophysiology. Both ischemic and hypoxic events are well-described, even with CPP values above 70 mm Hg.[11] Importantly, higher than appropriate CPP can quickly lead to hyperperfusion breakthrough and subsequently to tissue hyperemia and increased ICP.[12]

Cerebral Oxygen Monitoring

One of the tenets of neurocritical care therapy is the prevention of secondary tissue ischemia. To date, four methods exist to measure brain oxygenation: jugular venous bulb oxymetry, near infrared spectroscopy, brain tissue oxygen tension, and $^{15}O_2$ PET.

Jugular venous bulb oxymetry is based on the retrograde insertion of a fiberoptic oxymeter (Abbot Opticath, Abbott Laboratories, Chicago, IL) into the jugular vein with the tip placed into the jugular bulb with radiographic position confirmation, to continuously measure the oxygenation of cerebral venous blood return ($SjvO_2$).[13] The oxymeter needs to be recalibrated daily and is MRI compatible; the normal $SjvO_2$ range is 55% to 69%.[14] Cerebral venous oxygen saturation is the difference between cerebral oxygen delivery and the brain metabolic demand of oxygen ($CMRO_2$, given that the hemoglobin concentration, hemoglobin saturation, and hemoglobin dissociation remain unchanged). The $SjvO_2$ provides a direct measurement of CBF in patients with normal flow-metabolism coupling as it can detect hemispheric arterial hypoperfusion, that is, a reduction in oxygen delivery (CBF), or increase in demand, that is, in oxygen extraction (oxygen extraction fraction, OEF). A high $SjvO_2$ indicates the opposite, either a reduction in oxygen extraction (OEF) or an increase in oxygen delivery (hyperperfusion). As the hemoglobin concentration in arterial and venous blood is the same, and the difference in the amount of dissolved oxygen is usually minimal between arterial and venous samples (at low FiO_2), the ($AVDO_2$) can be estimated by comparing the difference between SaO_2 and $SjvO_2$, the

so-called cerebral extraction of oxygen, or CEO_2 (or, on other words $AVDO_2 = CMRO_2/CBF$, where $CMRO_2$ is the metabolic rate of oxygen consumption). The normal range of CEO_2 is 24% to 42%.[15]

The use of $SjvO_2$ is in three categories: as a prognostication tool, to adjust the optimal rate of hyperventilation, and to monitor for intraoperative and postoperative desaturation. After traumatic brain injury about one third of patients have jugular venous desaturations and the occurrence correlates with increased mortality.[16] In comatose patients, single episodes of low (<50%) $SjvO_2$ for >10 minutes correlate with an increase in mortality.[17] Experience proves that many desaturation events could have also been detected by monitoring ICP, mean arterial pressure, and systemic oxygen and end-tidal carbon dioxide ($ETCO_2$); however, $SjvO_2$ allows improved fine-tuning of cerebral oxygen balance. The titration of critical brain arterial perfusion thresholds can be guided by optimizing the $SjvO_2$ in an individual patient. Further, in patients with high $SjvO_2$ and reduced extraction fraction (CEO_2), hyperventilation (inducing reduction of cerebral blood flow from arterial constriction) can be titrated to achieving normal $SjvO_2$. Theoretically, such monitored hyperventilation will allow reduction in critically high ICP without inducing an abnormally low $SjvO_2$ that may otherwise further aggravate brain ischemia. Intraoperative use of jugular venous oxymetry identified frequent (up to 50%) desaturations during aneurysmal surgery for patients with subarachnoid hemorrhage[18] and during cardiac surgery (in 23%), the latter correlated with worse postoperative cognitive outcome.[19]

However, the limitations of this method are not solely the inherent risks of placing and maintaining the catheter. The probe is prone to artifacts and, importantly, jugular venous oxymetry only measures the global oxygenation of one hemisphere, hence, will not detect contralateral oxygenation problems or smaller, regional problems ipsilateral to the transducer. Reliability is further compromised by marked changes in arterial oxygen content and prone patient positioning. Additionally, a relative but small risk of infections, venous thrombosis, arterial puncture, and pneumothorax exists.[20] Further, it is useful to recalibrate the device not only on a regular basis (i.e., every day), but also when the device reading and a blood sample withdrawn from the catheter is >4% discordant.[13] In the hands of an expert clinician and with selection of the right patient population (i.e. head trauma, other injuries leading to diffuse cerebral edema, etc.) jugular venous oxymetry represents a very valuable clinical monitoring method.

Transcranial cerebral oxymetry is based on near infrared spectroscopy (NIRS), using the transmission and tissue absorption of near-infrared light (700 to 1000 nm), the latter commonly used in modern systemic oxygenation monitoring (i.e. positioning on ear lobe, fingers, or toes) as it provides a simple and cheap measure of hemoglobin saturation and systemic oxygenation. Transcranial cerebral oxymetry is based on similar principles and commercially available (NIRO series, Hamamatsu Photonics, Japan; INVOS series, Somanetics Corporation, Troy, MI, USA). These cerebral oxymeters are placed directly on the skull and measure oxygen saturation of the hemoglobin directly underlying the probe (rSO_2), that is, a mixture of venous and arterial blood and brain tissue. Normal rSO_2 values have been reported to be between 60% and 80%.[21] For example, the method has been used to monitor changes in cerebral oxygenation during carotid endarterectomy.[22] Other studies have found inconsistent results with respect to the method's predictive outcome values.[23,24,25] There is rather significant skepticism among experts in the reliability of this method. Not only does NIRS fail to differentiate between extra- and intracranial blood oxygenation sources, but also "normal" values were reported in studies using pumpkins, brain dead patients, and corpses.[26,27,28] Furthermore, the degree of scatter from infrared light is unpredictable among adult patients, especially when scalp hematoma or swelling is present. These disadvantages and monitoring inconsistencies have greatly limited cerebral NIRS for adults with brain injuries. Possible intracranial use of similar technology may become more useful, but becomes far more invasive.

Brain tissue oxygen tension (brain $PtiO_2$ or $PbtO_2$) directly measures the oxygenation of brain parenchyma using a small, flexible microcatheter inserted through a small burr hole into the white matter. The catheter is fixated at the burr hole site by a special bolt or may be tunneled and secured alternately. Two competing technologies are currently commercially available, Licox™, IntegraNeuroSciences, San Diego, CA, USA; Neurotrend™, Codman, Raynham, MA, USA). The Licox™ system uses polarography (using the so-called Clark electrode). In contrast, the Neurotrend™ employs optical luminescence to measure $PbtiO_2$, $PbtiCO_2$, and brain tissue pH. Both systems are generally MR-compatible except for the expected image artifacts. Normal values range at 40 mmHg and the measured volumes is estimated at 17 mm^3.[29,30] However, measurements will vary depending on the placement region and be highest in the cortex and hippocampus and lower in the white matter. Microcatheter placement can be into the region of interest and should reach into the white matter; the external connections can be

tunneled after craniotomy or placed through a single double or triple lumen bolt. Cerebral tissue oxygenation reflects largely tissue perfusion but also the local extraction fraction. Studies suggest that brain ischemia, defined as <18 mg/100g/min on xenon-CT, correlates with a $PbtO_2$ of 22 mm Hg using the Neurotrend™ system,[31] jugular bulb venous desaturation (threshold at 50%) correlated with a $PbtO_2$ of 8.5,[32] and ischemia determined by SPECT correlates with an average $PbtO_2$ of 10±5 mm Hg compared with values of 37±12 mm Hg in normal brain.[33] Low $PbtO_2$ values are frequently found immediately after head injury[34] (Figure 8) and when CPP is compromised in the setting of raised intracranial pressure.[35]

Low $PbtO_2$ has been shown to correlate with poor outcome after traumatic brain injury; for example, Zauner et al. found in patients with severe head injury that the mean $PbtO_2$ was 39±4 mm Hg, 31±5 mm Hg, and 19±8 mm Hg for good, moderate to severe disability, and poor outcome.[36] Further, episodes of 30 minutes or more of $PbtO_2$ <10 mm Hg appear to indicate poor outcome.[37] $PbtO_2$ monitoring has been applied during neurosurgical procedures, especially with approaches employing temporary arterial occlusions, where it indicates tissue hypoxemia more reliably than jugular venous oxymetry when appropriately placed into the tissue region at risk.[38] Conversely, in subarachnoid hemorrhage patients, the value of $PbtiO_2$ monitoring for the detection of vasospasm is rather due to its small sample volume and the regional heterogeneity of vasospasm; however, $PbtO_2$ values do improve with successful vasospasm treatment.[39] As expected and discussed further above, in regions with focal pathology jugular venous oxymetry is less sensitive than $PbtO_2$,[40] and in a larger study comparing jugular venous and brain tissue oxygenation global ischemia was detected at 64%, 70%, and 90% for monitoring at the jugular versus brain tissue versus both sites.[13] $PbtO_2$ will provide real-time measurements of autoregulation (and its impairment) and the effect of therapeutic interventions. Therefore, it is expected to have a clear impact in many patients with traumatic or larger focal, acute brain lesions. Further, $PbtO_2$ may facilitate early detection of worsening or expansion of ischemic areas, such as penumbra of ischemic or hemorrhagic stroke (Figure 9). $PbtO_2$ is a valuable monitoring parameter for multimondality monitoring of the acute injured brain, especially when it is integrated with systemic hemodynamic and oxygenation parameters such as MAP, CPP, $ETCO_2$, and others.

Cerebral Metabolism Monitoring – Intracerebral Microdialysis

Brain microdialysis monitors the biochemical environment of the extracellular space. Developed in 1966 as the first use of a dialysis membrane, modern microdialysis devices contain a blood capillary-like dialysis probe (~0.62 mm in diameter) which is inserted into the brain region of interest and infused (ultralow at 0.1 to 0.2 μL/min) using either lactated Ringers solution or normal saline. The saline equilibrates with the interstitial fluid to compensate for the difference in ionic and biochemical interstitial fluid components (usually of a size smaller than 10-20 kD) between the two spaces. The dialysate is extracted after equilibrium perfusion (usually after 10 to 60 minutes) and then analyzed by enzyme spectrophotometry or high-performance liquid chromatography at the bedside. Common measures included glucose, lactate, and pyruvate to monitor carbohydrate metabolism; glutamate as a reflection of ongoing cell injury; and glycerol and choline to indicate cell membrane breakdown. A variety of additional substances can be monitored with advanced microdialysis membrane equipment that allow permeation of substances up to 300kD, for example, urea, amino acids and peptides, cytokines, anitbiotics, nitrates and nitrites, and adenosine. The catheter is MRI-compatible and commonly fixated at the cranium via a bolt, tunneled through craniotomy site, or inserted and fixated through a simple burrhole. Referred insertion sites are located directly within or close to the injury focus or at a standardized right frontal lobe site (Kocher's point) in patients with global brain injury.

During hypoxemia and ischemia, lactate metabolism and glutamate release increase which can be reliably detected by microdialysis and is further supported with concomitant declines in monitored $PbtO_2$ and CBF. Metabolites referring to increased cellular membrane damage such as choline and glycerol often preceed permanent neurological injury. Much of the microdialysis experience has been gained from studying patients following traumatic brain injury,[41,42] subarachnoid hemorrhage and clinical vasospasm,[43] intracerebral hemorrhage,[44] and intraoperatively.[45] Increases in the lactate/pyruvate ratios indicate incomplete glucose metabolism and ischemia and predict poor outcome in traumatic brain injury. Many other variables and ratios are currently under investigation in various neurosurgical and cerebrovascular patient populations, especially with respect to their prognostic value and potential reversibility of biochemical abnormalities under therapeutic maneuvers. Generally, observing the trends of microdialysis parameters seems to be more academic than simply applying absolute numerical values for each individual value. Cerebral microdialysis provides a

powerful research instrument, that when coupled to other neuromonitoring technology, stands to teach neurocritical care physicians the cellular and molecular pathophysiology of brain injury and the direct impacts of our therapeutic maneuvers.

Transcranial Doppler Ultrasound

Several important, continuous, flow-dependent variables of the cerebral arterial tree can be reliably and noninvasively assessed by means of transcranial Doppler sonography (TCD). For example, TCD can yield a noninvasive ICP monitoring method to identify and monitor the pressure effects of unilateral hemispheric mass lesions indicated by a decrease in ipsilateral mean flow velocities and reduced ipsilateral-to-contralateral pulsatility index ratio due to increases in ipsilateral pulsatility.[46]

In addition, several TCD examination methods have been described to access cerebral autoregulation. Most are not feasible to be employed for continuous monitoring. However, the technology allows for: a) assessments of cerebral autoreactivity using relative changes of the arterial carbon dioxide concentrations which inversely correlates with changes in cerebral flow velocity profiles when vascular reactivity is preserved;[47] this leads to ICP increases when reactivity has been exhausted;[48] b) measurement of middle cerebral artery flow velocities during iatrogenic increases in mean arterial pressure and expression of the rise as autoregulatory reserve by dividing the vascular resistance by the percentage rise of CPP [(CPP/FV)/CPP];[49] c) delineation of the phase shift of superimposed MCA flow velocities, and arterial pressure and respiratory curves where a zero degree phase shift indicates lack of autoregulation, that stands in contrast to a 90º phase shift indicating preservation of autoregulation;[50] and d) absence of cerebral autoregulation if a stepwise deflation of compressive leg cuffs leads to a parallel decline in bilateral MCA flow velocity.[49] It is of note that none of these methods as been accepted into regular clinical practice as these tests are time consuming and operator dependent and yet have not been rigorously evaluated for their predictive clinical value. We do not advocate testing for the transient hyperemic response identified on MCA flow monitoring after manual, temporary ipsilateral extracranial internal carotid artery compression.[51]

While there are many complicated techniques for measuring advanced intracranial hemodynamics with TCD that at present appear too cumbersome to be routinely useful in the NSICU, TCD represents a powerful tool that continues to increase its clinical utility, including

measurement of flow velocities to screen for and follow vasospasm after subarachnoid hemorrhage, altered perfusion and flow dynamics following branch stroke, revascularization and re-establishment of blood flow following administration of thrombolytic medications either intravenous or endovascularly delivered, determination of mass lesions at the bedside in patients too critically ill to be transported to imaging centers, and flow diagnosis of cerebral circulatory arrest, among others.

Continuous EEG (CEEG) and Evoked Potentials (CEP) Monitoring

Prolonged monitoring of electrical cerebral activity, with and without video surveillance, has gained increasing favor in the neurocritical care setting. Several indications, some of them more distinct than others, support the argument to perform continuous electroencephalography (CEEG) monitoring. Spot and continuous EEG facilitates diagnosis and augments streamlined care in patients with known or suspected seizure disorder, especially if the level of consciousness is altered by brain injury or medications, patients during and after status epilepticus, patients with difficult to characterize motor abnormalities such as tremor, unusual or repetitive ocular, facial, or oropharyngeal movements, and patients with unexplained or abrupt dysautonomia unexplained by the primary injury mechanisms. Further, EEG allows determination of level of consciousness in patients suffering paralysis or requiring continous sedation, and titration of induced coma to burst suppression, detection of delayed ischemic events after aneurysmal or traumatic subarachnoid hemorrhage. While we generally do not use EEG for brain death determination, it remains a helpful adjuvant for prognostication in severely brain injured victims.

Traditionally, CEEG was first employed in status epilepticus patients and in the operating room during carotid endarterectomy.[52] Other earlier reports identified a correlation between repetitive slow waves or 'axial bursts' as indicator for delayed ischemia in patients with clinical and angiographic vasospasm.[53] More modern approaches include quantitative analyses of epochs of stored data allowing trend analyses to indicate changes suggestive of regional ischemia in subarachnoid hemorrhage patients, among them, reduction of total power, relative alpha variability, and post-stimulation alpha/delta ratio. Further, cortical spreading depression can be detected, defined as prolonged, repeated, slow electrical depolarizations possibly indicative of ongoing focal injury.[54] However, CEEG has practical limitations beyond its non-specificity and variable sensitivity, such as difficulties to obtain real-time data interpretations, MRI-

incompatibility of most surface electrodes, applicability problems post craniotomy and during concurrent invasive brain monitoring, environmental artifacts, and need for continuous technical staffing. In contrast, increasing availability of networking, power spectrographic displays compressing hours of data into single time frames, accessibility over the internet, and software supporting recognition of event-related electrographic changes make CEEG a useful tool in selected cases even in non-academic critical care settings.

Evoked potential recordings are very useful in prognostication after serve head trauma, especially in patients remaining in coma after cardiac arrest. For example, somatosensory evoked potentials (SSEP's) are frequently used in postcardiac arrest patients. Normal conduction times of the N13 and N20 components indicate a 60% chance of good neurologic outcome after 12 months in patients with severe head trauma. A delayed component reduces this percentage by more than half, and their absence make death and severe disability much more likely.[55] Bilateral absence of the N20 cortical components, together with a lack or severe impairment of brainstem reflexes strongly support an overall poor prognosis.[56] Additionally, we use continuous somatosensory and auditory evoked potentials to monitor the brainstem function in comatose patients at risk for downward displacement (central herniation) from bilateral hemispheric brain swelling leading to high, intractable ICP. Recently, a description of combined EEG and EP monitoring became available.[57]

Multimodal Neuromonitoring

Ongoing brain tissue ischemia and hypoxia is one of the common pathophysiologic mechanisms for worsening brain injury in the acute and subacute phase of trauma, intracerebral and subarachnoid hemorrhage, ischemic stroke, post-cardiopulmonary arrest, and many other acute neurological illnesses and deterioration.

New and exciting bedside brain monitoring techniques are available providing a crucial, moment-to-moment update of the hemodynamic, electrical, and cellular environment of the injury site and its surrounding, potentially salvageable tissue areas (Table 1). While currently no single monitoring parameter provides reliably sufficient crucial information to detect secondary injury there is a definite advantage of combining and integrating the information of a choice of monitoring devices to improve outcome in brain injuries. New devices reducing invasive access continue to emerge. Hummingbird™ (Innerspace Incorporated, Tustin, CA, USA) provides a

cannulated access system to place various different neuromonitoring devices, depending on the individual patient's circumstances and the desired neuromonitoroing parameters. Other such technologies are in development and will offer the advanced neurocritical care practitioner the ability to acquire patient data more easily and safely.

We currently can measure cerebral blood flow both quantitatively and qualitatively in real-time and integrate the flow values with tissue oxygenation data and cellular performance measures from microdialysis in order to carefully track brain tissue 'performance measures' and therapeutic interventions. However, the true strength and depth of brain monitoring comes not as much from the addition of single parameters, but rather from novel approaches to analyze the relationship of the parameters in order to detect trends indicative of functional worsening and to allow interfering therapeutically in proactive rather than reactive approach. Multimodality neuromonitoring, neuroimaging, and neurophysiologic decision support systems are already an indispensible tool for the neurocritical care physician. Computer-assisted graphical analyses are already improving the patient's benefits from multimodal monitoring and we need to define further our insights and understanding into the critical conditions ultimately leading to worsening brain injury.

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Figure Legends

Figure 1. Multimodal monitoring of patients in the neuroscience intensive care unit requires compilation of information from various patient care systems and devices, as well as the standard hospital based data repositories. By collecting information centrally, data may more accurately and rapidly translate into answers to research questions, lead to more appropriate coding and billing for services and procedures, and improve quality assurance investigation, all of which lead to a more functional environment with improved patient outcomes and delivery of care.

Figure 2. Advanced neuromonitoring requires balanced evaluation and management of systemic and intracranial physiologic measures. For each value, one or more monitoring, laboratory, or imaging technologies exists to avoid the pitfalls leading to poor outcomes. Stability leads to improved cerebral perfusion and cerebral oxygen delivery. Loss of any one component may inadvertently facilitate patient deterioration.

Figure 3. The intracranial pressure (ICP) waveform in normal (top) and elevated (bottom) pressure conditions. The percussion wave (P1) represents arterial pulsations. The rebound wave (P2) reflects the intracranial compliance. The dichrotic wave (P3) represents venous pulsation. As ICP increases, the amplitude of P2 increases more than P1, indicating a reduced cerebral compliance.

Figure 4. Idealized optimization of the cerebral perfusion pressure (CPP) with augmented blood pressure. As the intracranial pressure (ICP) increases, the CPP decreases at any stable systemic blood pressure (CPP = MAP - ICP). Blood pressure augmentation facilitates a return to normal or optimal CPP. Such augmentation may be accomplished via fluids, colloids, or vasopressors.

Figure 5. The ICP curve demonstrates the effect of an expanding intracranial mass (i.e. tumor, hemorrhage, hydrocephalus) on the intracranial pressure. The ICP remains under tight control via CSF diversion and cerebral blood flow autoregulation until a critical point, followed by rapidly increasing ICP. This critical point indicates a key target for rapidly therapeutic

intervention. Multimodal neuromonitoring facilitates avoidance of reaching this emergency juncture.

Figure 6. The impact of intracranial (ICP), perfusion (CPP), and arterial blood gas pressures (PaO_2 and $PaCO_2$) on the cerebral blood flow (CBF). The schematic curves demonstrate that under the wide range of normal pressures, CBF maintains approximately 50 mL/100g/min.

Figure 7. Cerebral blood flow (CBF) and intracranial pressure (ICP) are maximally controlled over a broad range of normal cerebral perfusion pressures (CPP, 50-150 mm Hg) through complex autoregulatory mechanisms. Below the autoregulatory zone, ineffective cerebral perfusion and intact pressure regulation leads to vasodilation to facilitate raising the CPP. Normal brain compliance (solid line) allows for functional autoregulation to maintain sufficient CPP. Beyond the autoregulatory zone, therapeutic reduction in CPP reduces overload of cerebral blood volume that otherwise leads to increased ICP. Maintenance of vessel tone within this range, allows for stable blood volume delivery. However, in states of reduced intracranial compliance (dashed line), poor compliance also leads to less effective autoregulation and often notably reduced CBF at an otherwise normal CPP. Thus, global ICP and CPP measurements are inadequate and more elaborate monitoring of additional physiologic parameters becomes necessary.

Figure 8. Schematic representation of brain tissue oxygenation ($PbtO_2$) in diffuse brain injury. Monitor location facilitates both diagnostic and therapeutic maneuvers. In this idealized curve of a $PbtO_2$ sensor placed in an apparently uninjured location following diffuse brain injury, the initially low oxygenation indicates the extent of global injury. This may be seen clinically in only a delayed fashion. By early recognition of such a phenomenon, appropriate therapeutic maneuvers may be performed to raise the $PbtO_2$ to normal (>20 white matter, 35-40 gray matter) and thus improve tissue survival in salvageable zones.

Figure 9. Schematic representation of brain tissue oxygenation ($PbtO_2$) in a pericontusional area. Monitoring allows early recognition of physiologic deterioration as a contusion enlarges, manifest by a remarkable decrease in the $PbtO_2$. Focal metabolic changes may not be detected

by global monitors of cerebral function, such as ICP or $SjvO_2$ until much later, possibly delayed beyond outside of a therapeutic time window.

Table 1. Neuromonitoring devices and reference values commonly employed in the neuroscience intensive care unit.

Abbreviations: ACA, anterior cerebral artery; CBF, cerebral blood flow (mL/100g brain/min); CO_2R, CO_2 Reactivity; CPP, cerebral perfusion pressure (mm Hg); EDV, end diastolic velocity (cm/s); EEG, electroencephalography; ICP, intracranial pressure (mm Hg); L/P, lactate-pyruvate ratio; LR, Lindegaard Ratio Index; MCA, middle cerebral artery; MFV, mean flow velocity (cm/s); OEF, oxygen extraction fraction; $PbtO_2$, brain tissue oxygen tension (mm Hg); PCA, posterior cerebral artery; PI, pulsatility index (PSV-EDV/MFV); PSV, peak systolic velocity (cm/s); SjO_2, jugular venous oxygen saturation (%); SAH, subarachnoid hemorrhage; VA, vertebral artery.

Figures

Table 1.

Monitoring Technology	Invasive	Physiologic Parameters	Normal Ranges	Pathology
ICP monitor	Yes	ICP CPP	<20 mm Hg ≥60 mm Hg	≥20 mm Hg <60 mm Hg
Brain tissue oxygen monitor (Licox™, Neurotrend™)	Yes	$PbtO_2$ $PbtCO_2$ Brain pH Brain temperature	20 mm Hg white matter 35-40 mm Hg in gray matter 43-50 mm Hg 7.2 37˚C	<20 mm Hg, cerebral hypoxia <8 mm Hg hypoxia/ischemia >60 mm Hg, brain hypercarbia <7.15 tissue acidosis <36.8˚C or > 37.2˚C
Jugular venous oximetry	Yes	SjO_2	50-75%	<50%, increased OEF, ischemia >75%, reduced OEF, hyperemia
Cerebral blood flow	Yes	CBF	50 mL/100g/min	<20 mL/100g/min leads to loss of neuronal function and ischemia
Cerebral microdialysis	Yes	Glucose Lactate Pyruvate Glutamate Glycerol Lactate/Pruvate ratio	1170 ± 900 μmol/L 2900 ± 900 μmol/L 166 ± 47 1.6 ± 16 μmol/L 82 ± 44 μmol/L 10-40	Increased glutamate and lactate are the earliest microdialysis markers of ischemia, followed by increased lactate/pyruvate ratio, decreased glucose, and increased glycerol. L/P >40 indicates ischemia
Continuous EEG	No	Brain electrical activity Epileptiform activity	Alpha/Delta ratio < 50% No epileptiform discharges Normal reactivity to stimuli	Alpha/Delta ratio > 50% Epileptoform discharges Unreactivity to stimulation
Transcranial Doppler Ultrasound (TCD)	No	MFV Pulsatility Index CO_2 Reactivity Lindegaard Ratio	MCA 30-75 cm/s ACA 20-75 cm/s PCA 15-55 cm/s VA 13-66 cm/s PI 0.9-1.2 in any vessel $CO_2R \geq 2\%$ increase LR < 3:1	MCA MFV 140-200 cm/s, indeterminate probably of vasospasm after SAH MCF MFV > 200 cm/s, high probability of vasospasm after SAH PI ratios Ipsilateral/Contralateral > 1.25 suspicious for compartmentalized ICP or mass effect $CO_2R < 2\%$ increase LR > 3:1 mild vasospasm LR > 6:1 severe vasospasm

Figure 1.

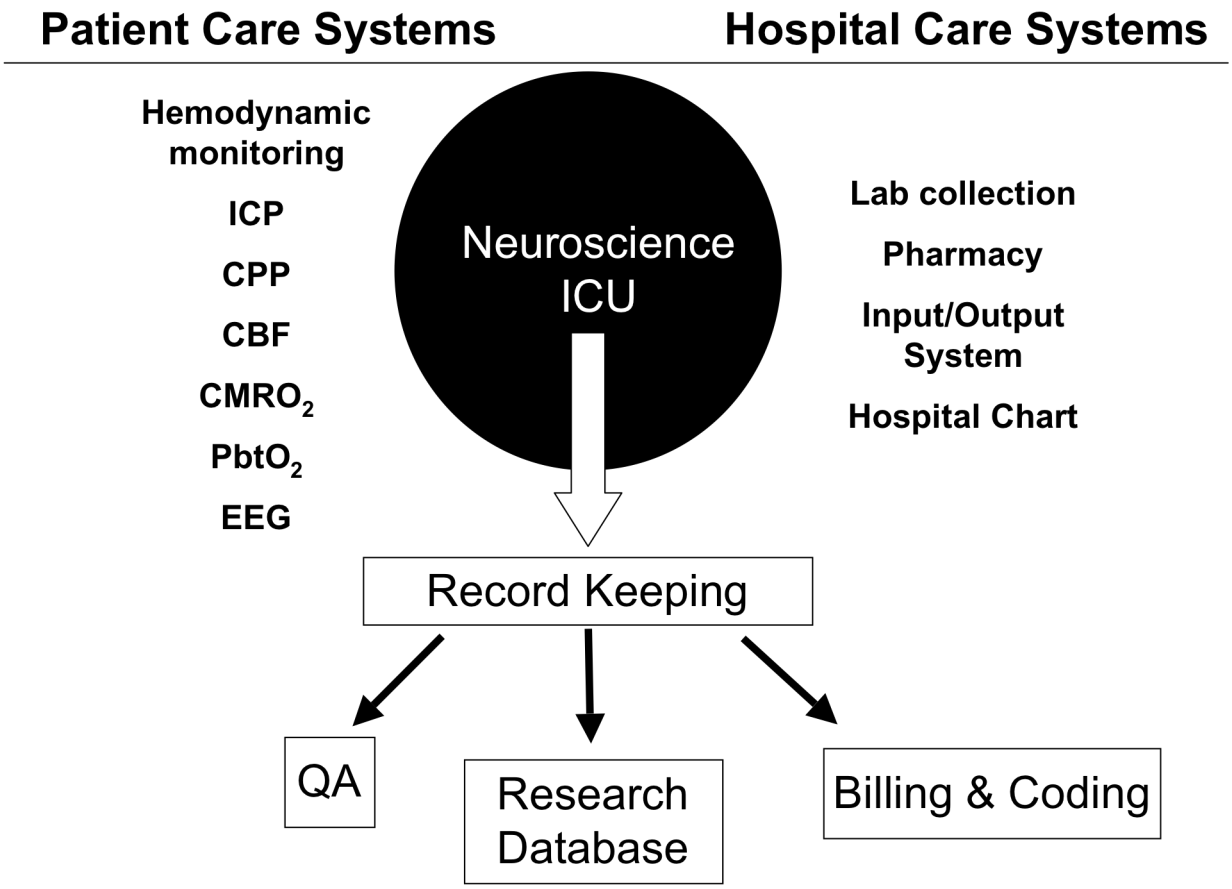

Patient Care Systems
Hospital Care Systems
Hemodynamic monitoring
ICP
CPP
CBF
CMRO2
PbtO2
EEG
Neuroscience ICU
Lab collection
Pharmacy
Input/Output System
Hospital Chart
Record Keeping
QA
Research Database
Billing & Coding

Figure 2.

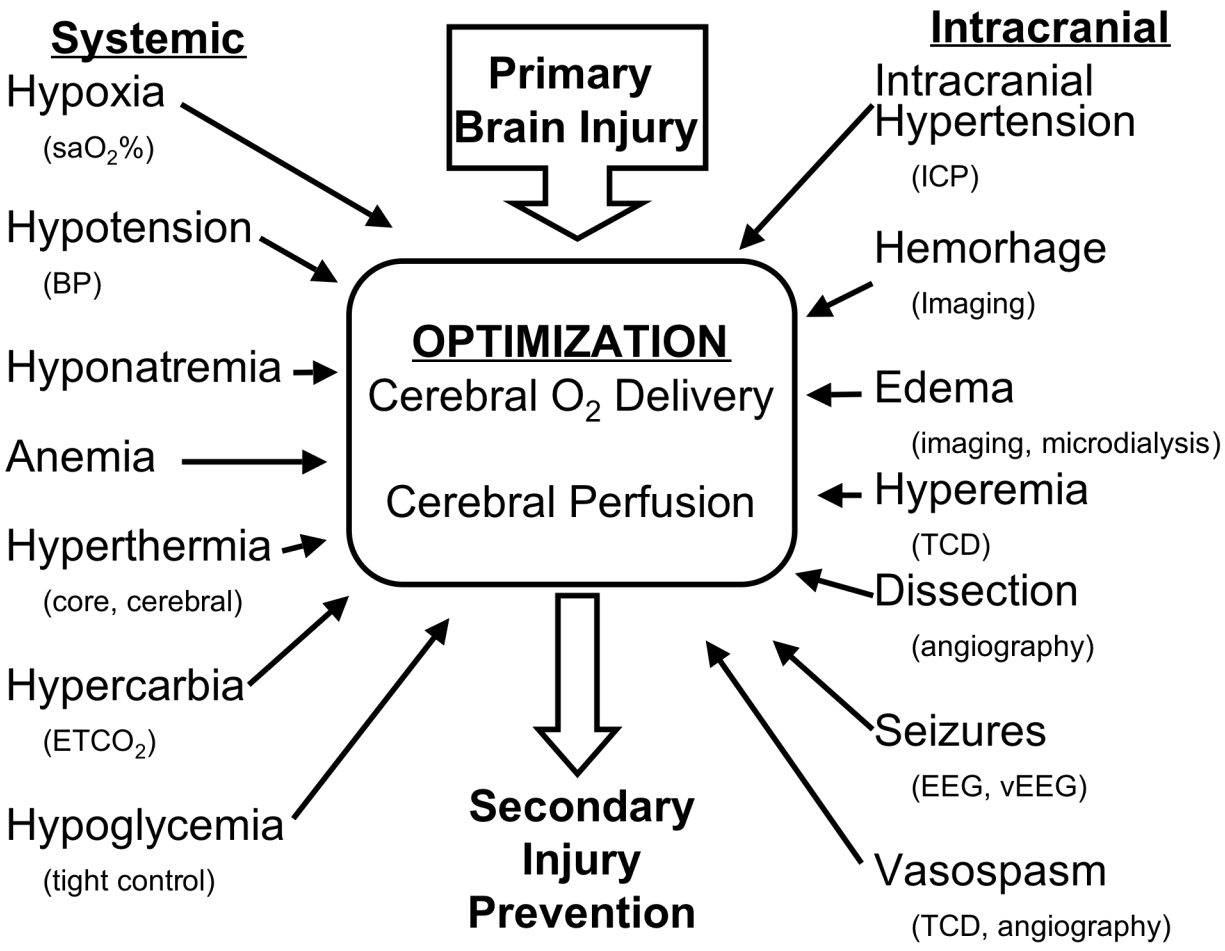

Systemic
Hypoxia
(saO_2%)
Hypotension
(BP)
Hyponatremia
Anemia
Hyperthermia
(core, cerebral)
Hypercarbia
($ETCO_2$)
Hypoglycemia
(tight control)
Primary Brain Injury
OPTIMIZATION
Cerebral O_2 Delivery
Cerebral Perfusion
Secondary Injury Prevention
Intracranial
Intracranial Hypertension
(ICP)
Hemorhage
(Imaging)
Edema
(imaging, microdialysis)
Hyperemia
(TCD)
Dissection
(angiography)
Seizures
(EEG, vEEG)
Vasospasm
(TCD, angiography)

Figure 3.

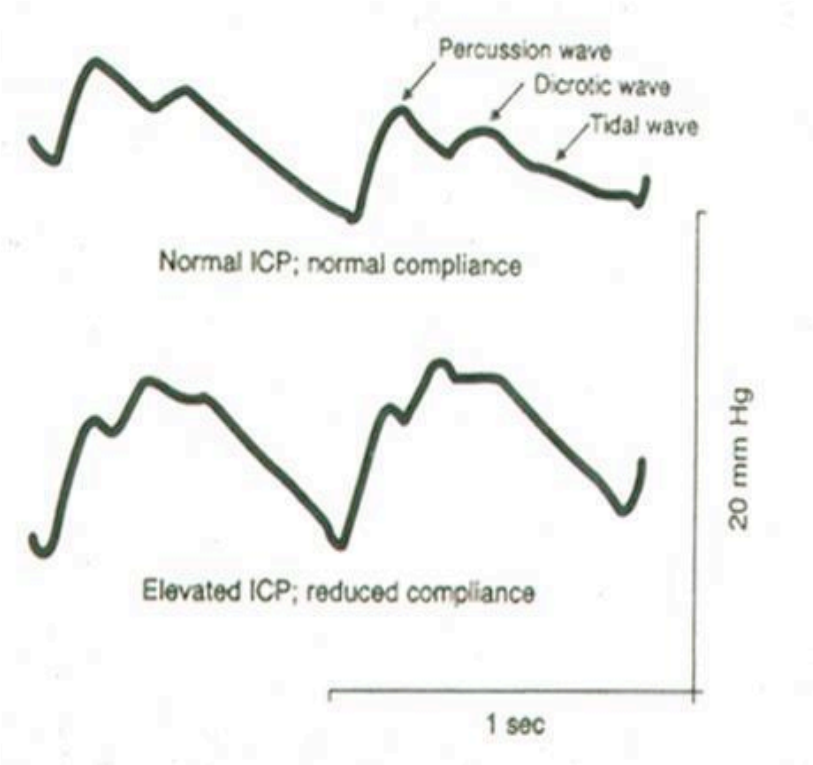

Percussion wave
Dicrotic wave
Tidal wave
Normal ICP; normal compliance
Elevated ICP; reduced compliance
20 mm Hg
1 sec

Figure 4.

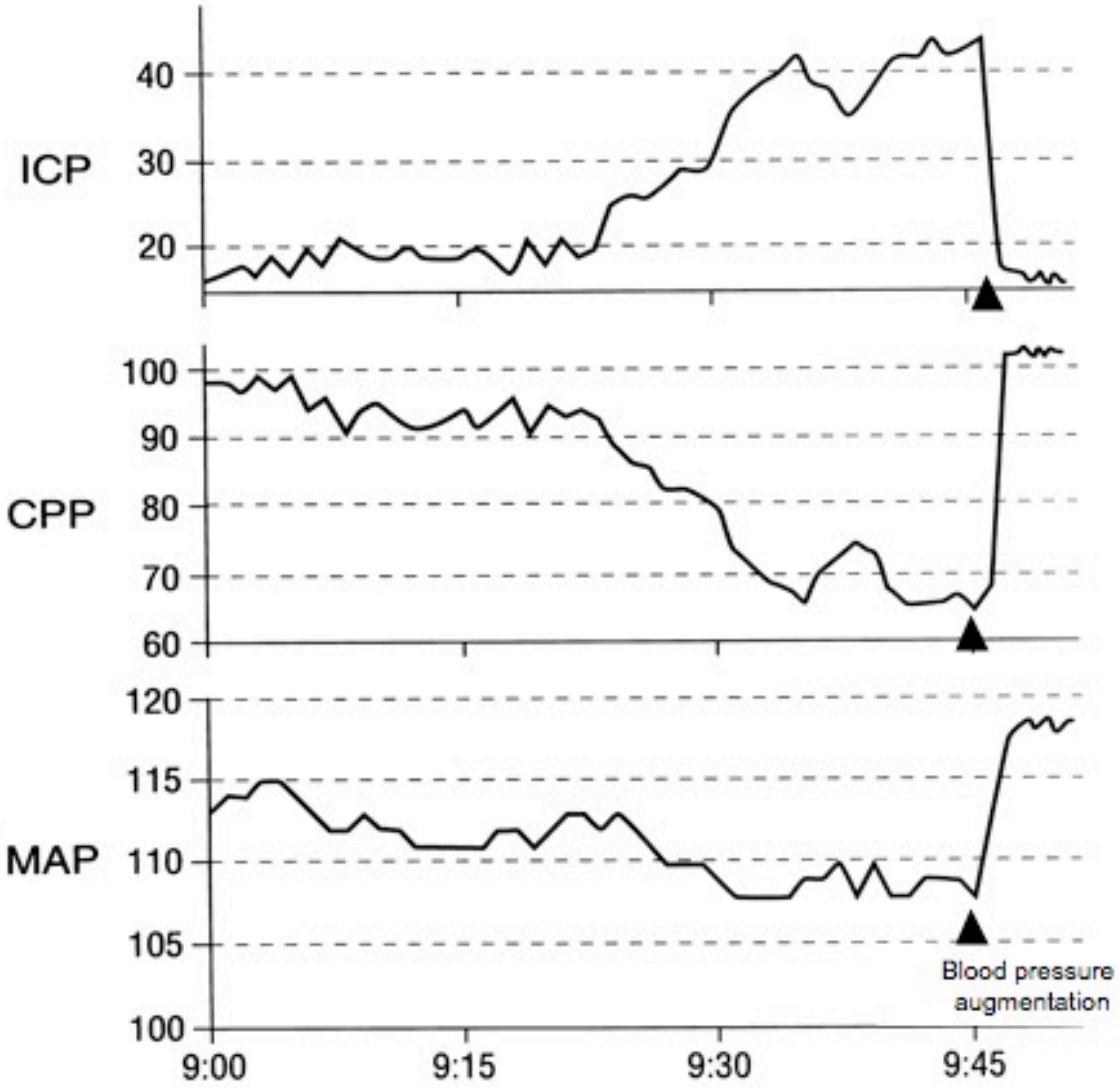

ICP
40
30
20
CPP
100
90
80
70
60
MAP
120
115
110
105
100
Blood pressure augmentation
9:00
9:15
9:30
9:45

Figure 5.

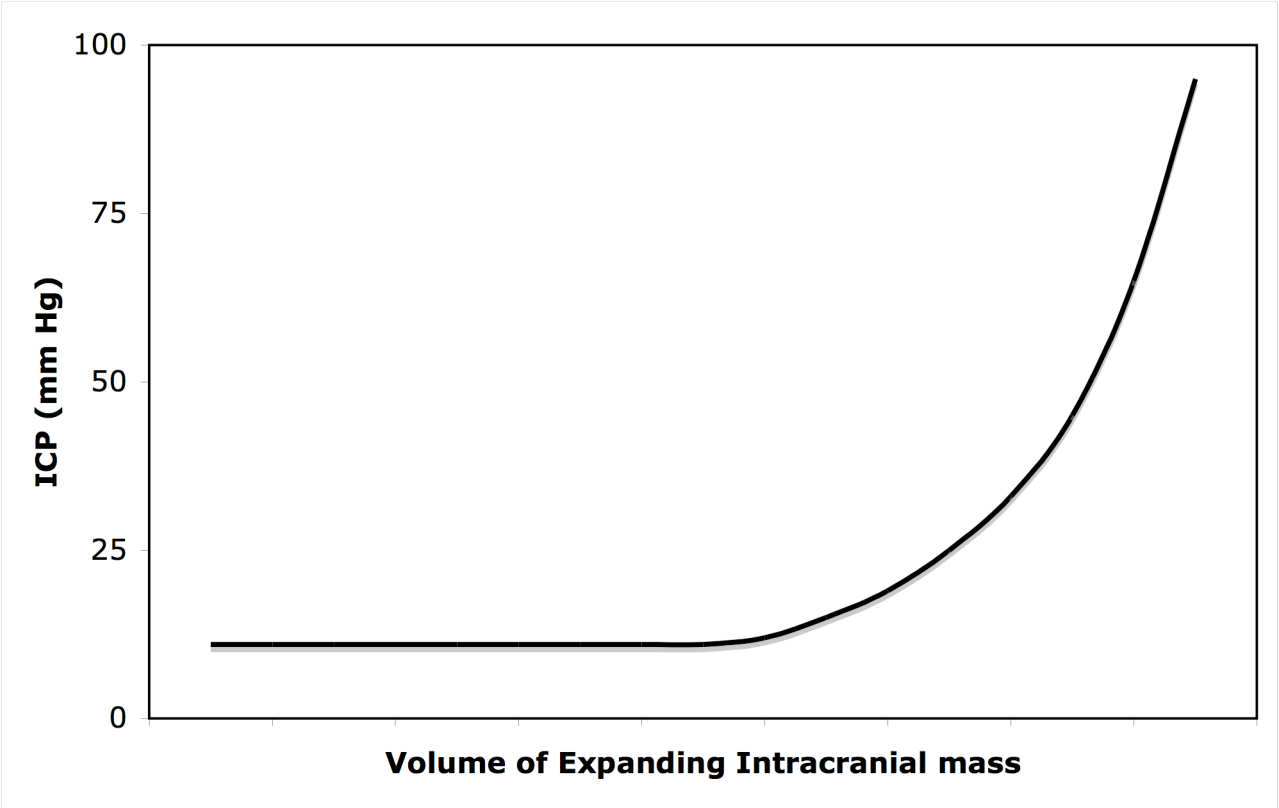

100
75
50
25
0
ICP (mm Hg)
Volume of Expanding Intracranial mass

Figure 6.

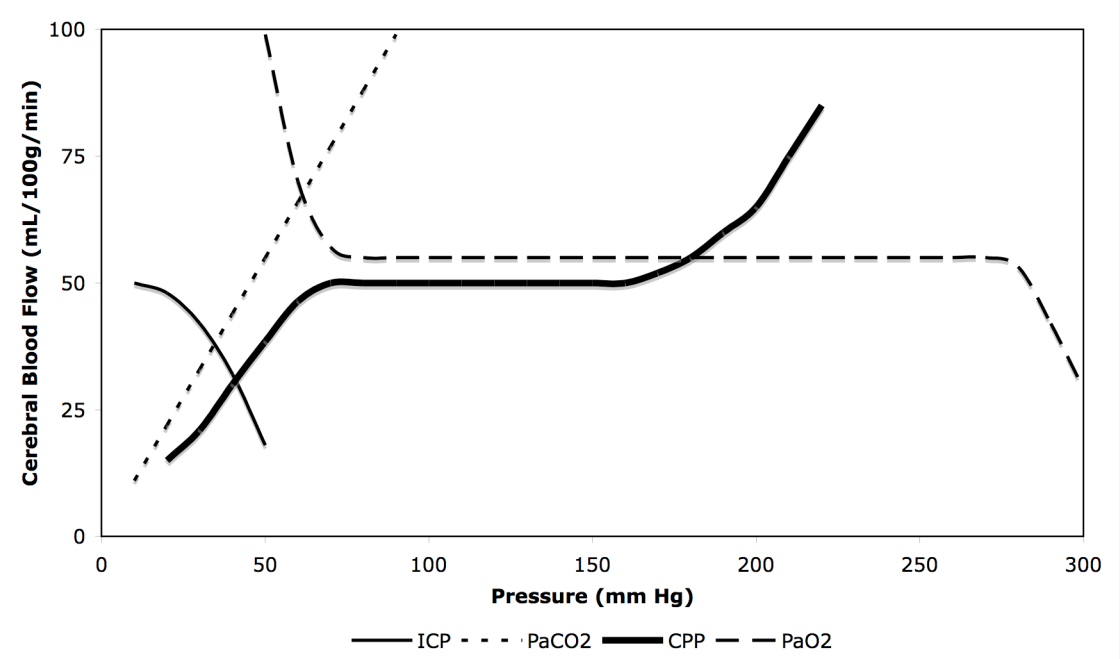

100
75
50
25
0
Cerebral Blood Flow (mL/100g/min)
0
50
100
150
200
250
300
Pressure (mm Hg)
ICP
PaCO2
CPP
PaO2

Figure 7.

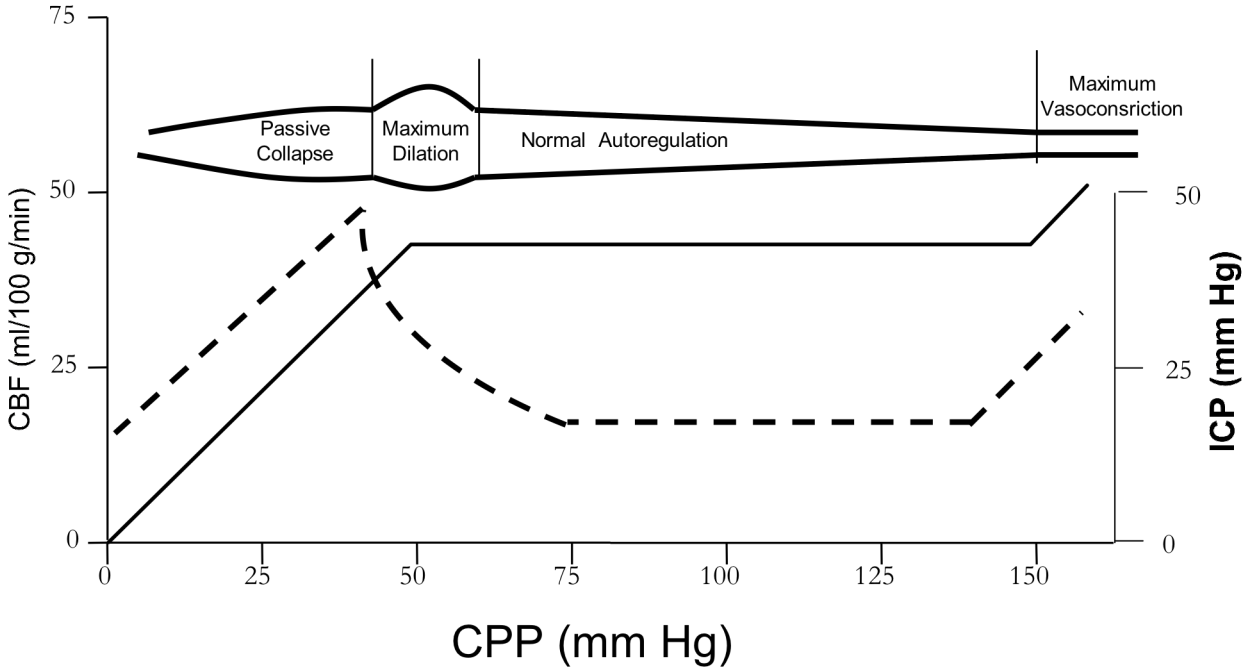

75
50
25
0
CBF (ml/100 g/min)
Passive Collapse
Maximum Dilation
Normal Autoregulation
Maximum Vasoconsriction
50
25
0
ICP (mm Hg)
0
25
50
75
100
125
150
CPP (mm Hg)

Figure 8.

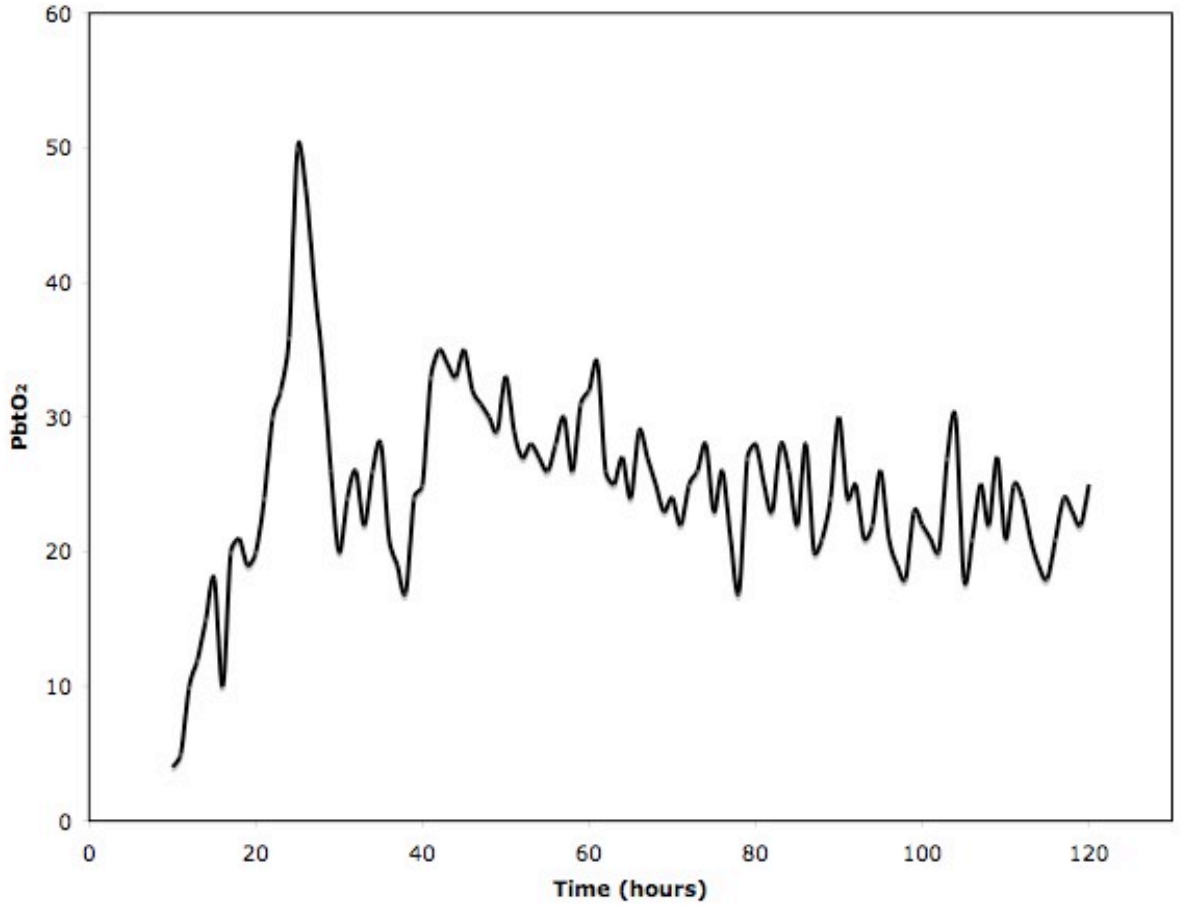
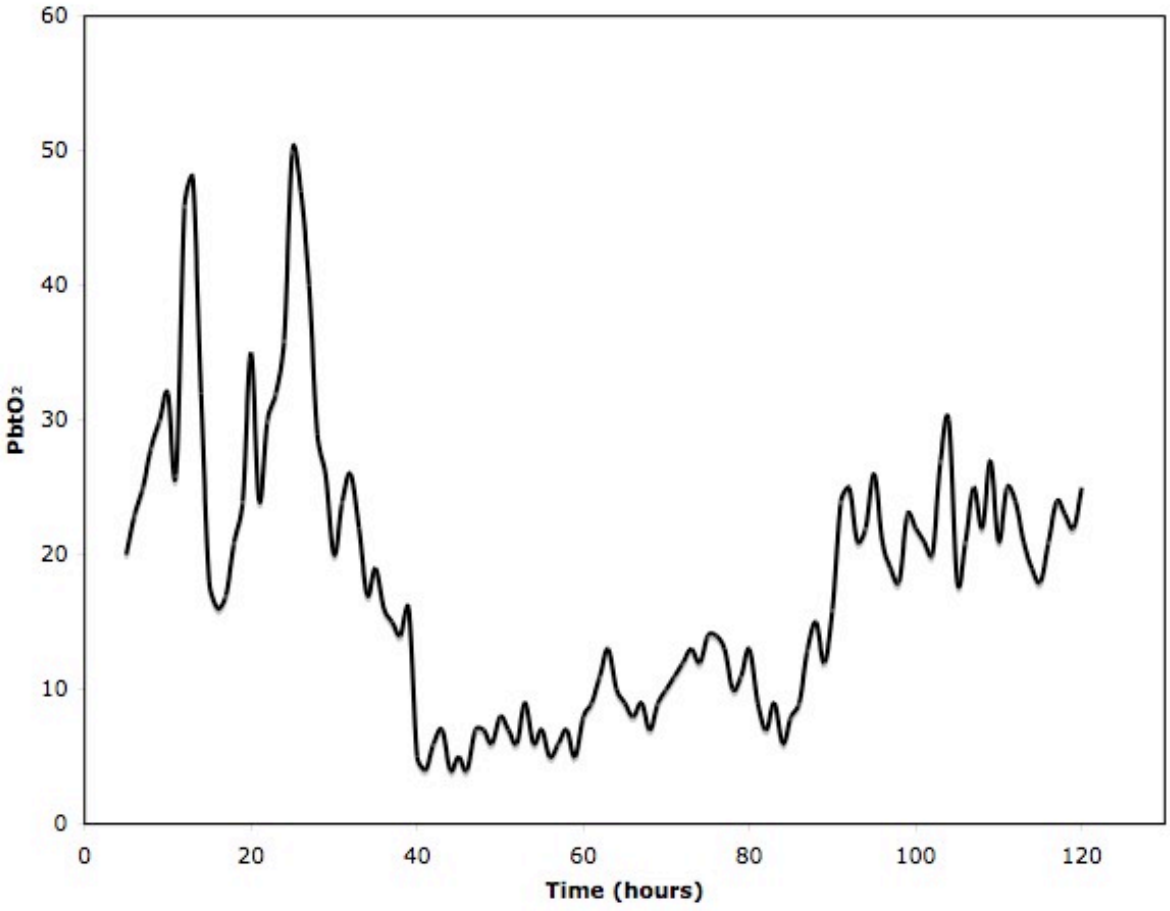


Figure 9.



Intraventricular Administration of Recombinant Tissue Plasminogen Activator to Treat Basal Ganglia Hemorrhage with Intraventricular Extension

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ABSTRACT

INTRODUCTION:

Basal ganglia hemorrhage with intraventricular extension that might be complicated with hydrocephalus has been associated with high morbidity and mortality rates. Mortality associated with ICH with IVH is reported from 32 to 44%, and if involves all four ventricles, the mortality is reported as high as 91%.[3,7,15-17] External ventricular drainage (EVD) has been the conventional treatment used for associated hydrocephalus and ICP management; however, multiple studies have failed to demonstrate neurological improvement with EVD placement alone. Nevertheless, other studies have shown rapid clot resolution and improved clinical outcomes with the administration of intraventricular fibrinolytic agents. Our study examines the safety (rebleeding and infection) and neurological outcome in patients who received intraventricular rtPA after ICH with IVH.

METHOD:

Prospective, multi-center data collection was reviewed of patients presenting with spontaneous basal ganglia hemorrhage and intraventricular extension requiring ventriculostomy who received serial intraventricular rtPA or preservative free saline flush post-hemorrhage. Serial head CT scans were performed for quantitative determinations of hemorrhage volumes using the Le Roux scale initially and at termination of the intraventricular injections. Patient outcomes were analyzed using the change in Glasgow coma scale (GCS) after 5 days of intraventricular medication administration, and Karnofsky performance status scale at 30 and 60 days from completion of administration of the drug.

RESULTS:

Significant resolution of clot on CT scan was observed ($p = .02$) in the rtPA group compared to the preservative free saline flush group. Overall, 30% decrease in mortality was observed in the rtPA group when compared to the preservative free saline flush group. The change in Glasgow coma scale failed to show a significant clinical difference between the rtPA group and the preservative free saline flush group at the end of the 5-day drug administration period ($P > .05$); however, Karnofsky scale illustrated significant progressive improvement ($P = .04$) at thirty days and sixty days in the rtPA group. In the rtPA group, one patient experienced reoccurrence of bleeding, we suspect secondary to uncontrolled hypertension. None of the patients had re-hemorrhaged in the preservative free saline flush group. Neither group developed an infection throughout the study.

CONCLUSION:

Intraventricular administration of rtPA shows promising results in safely resolving IVH, maintaining patency of ventricular drainage catheter, decreasing hydrocephalus, and improving neurological outcome and mortality.

INTRODUCTION

Intraventricular hemorrhage (IVH) has significantly contributed to the morbidity and mortality after intracerebral hemorrhage.[1-5] IVH occurs in 10 – 40 % of all intracerebral hemorrhages (ICH), with 70% of these spreading from other areas, the most common being hypertensive hemorrhage in the basal ganglia and thalamus.[5-9,32] When intraventricular blood and CSF is inadequately drained, there is an increase in intracranial pressure (ICP). ICP greater than 20 mmHg is detrimental to patients' prognosis.[7,10-12] Studies have shown this results in decreased cerebral blood flow, and damage to the ependymal and subependymal layers of the brain and the brain stem.[6,7,13,14] Mortality associated with ICH and IVH is reported from 32 to 44%, and if involves all four ventricles, the mortality is reported as high as 91%.[3,7,15-17]

Traditionally, active treatment of IVH involves placement of external ventricular drains; however, multiple studies have shown external ventricular drain (EVD) placement alone does not improve outcome.[4,7,18-20] Nevertheless, other studies have shown rapid intraventricular clot resolution and improved clinical outcomes with the administration of intraventricular fibrinolytic therapy. Recombinant tissue plasminogen activator (rtPA) has shown promising results.[6,7,17,21-24] rtPA is naturally released by the vascular endothelial cells, an increase in its release is observed in IVH but not adequate enough to allow rapid resolution of the IVH.[15,25-27] Our prospective, multi-center data collection was reviewed to examine the neurological outcome of patients with IVH from hypertensive basal ganglia hemorrhage receiving standard intraventricular rtPA versus those whose EVD was flushed with preservative free saline serially to ensure patency of the EVD . The data were compared using the Student's t test. The study was approved by the Institutional Review board (Protocol #: 07-21).

METHOD

Data was collected on total of 50 adult patients with history of hypertension and spontaneous basal ganglia hemorrhage with intraventricular extension requiring ventriculostomy, 25 patients for the rtPA group and 25 patients for the preservative free saline flush group. The mean age of patients in the rtPA group was 59.4 (range: 43-83; 18 males, 7 females) and the preservative free saline flush group was 65.2 (range: 45-92; 15males, 10 females) ($p = .17$). All of the hemorrhages were related to hypertension and median GCS score on admission was 4T in both groups (range: 3-8T). We followed our treatment protocol of placing a EVD in patients with GCS less than or equal to 8. Aggressive management of blood pressure was maintained throughout their admission to maintain systolic blood pressure less than 160 mmHg. The hemorrhage was diagnosed on CT scan and was followed with serial CT scans. Table 1 shows the grading system proposed by Le Roux that was used to quantify the severity of the IVH.[28]

This scale involves qualitatively grading each ventricle (total four ventricles) from scale one to four and summing the results to give maximum score of 16. Patients with basal ganglia ICH with IVH, and were GCS scores 3 – 8 and had placement of EVD with ICP monitor were included in the study to receive rtPA or preservative free saline flush serially. Exclusion criteria included anyone with age less then 18, systemic clotting disorders, cerebral vascular abnormalities and no history of hypertension.

The group received approximately 3ml of preservative free saline flushes or 2mg of rtPA mixed w/ 2.2ml of sterile water per manufacturer's instructions (Genentech, Inc., South San Francisco, CA). The preservative free saline or the rtPA was administered at approximately 24-hour intervals for an average of five days. The medications were administered through the side port of the ventricular drainage catheter slowly to avoid increase in ICP. ICPs were monitored before and after the administration of the medications. The intraventricular catheter injections were performed using standard sterile technique and consisted of draining sufficient amount of CSF prior to the injections. The rtPA injections were followed by 1ml of preservative free saline. The drain was closed for 30 minutes and reopened to drain at the 0mmHg at the external auditory canal. The drainage was analyzed for infection every other day with CSF sampling performed using sterile technique.

The resolution of clot was recorded using the Le Roux grading system.[28] The patient outcome was analyzed using the change in Glasgow Coma Scale (GCS) at completion of the 5-day drug administration period and then, Karnofsky scale[22] at 30 and 60 days. We also recorded any occurrence of complications.

Table 1

Le Roux Scale for grading IVH[28]

1	Trace of blood
2	less than half of the ventricle is filled with blood
3	Greater than half of ventricle is filled with blood
4	Ventricle is filled with blood and expanded

Each ventricle is graded separately (n = 4) and the scores are added from each of the four ventricles (Max = 16).

RESULTS

Over the five days of the intraventricular rtPA injections, significant resolution of clot on CT scan was observed ($p = .02$) (Figure 1). Overall, in the rtPA group sixty percent more resolution of clot was observed based on the Le Roux scale. The initial Le Roux score averaged approximately 14 in both groups; however, post-administration scores were 5 and 9 for the rtPA and preservative free saline flush group, respectively. In two patients, complete resolution of the clot was observed in the rtPA group and none in the preservative free saline flush group (Figure 2 & 3). In both groups there were a number of patients with high post-administration Le

Roux scores because the patients died. This is reflected in the Figure 2 and 3 as no change from initial presentation in their Le Roux score and GCS score.

Overall, 30% decrease in mortality was observed in the rtPA group when compared to the preservative free saline flush group. In addition, increased mortality was observed at 30-day and 60-day follow-up in the preservative free saline flush group (4 and 4 patients) when compared to the rtPA group (2 and 2 patients). Eventhough, the change in GCS score failed to show a significant difference between the rtPA group and the preservative free saline flush group at the end of five day drug administration period ($P > .19$), the Karnofsky scale illustrated significant progressive improvement ($P = .04$). On average, patients in the rtPA group's Karnofsky performance status scores were double the Karnofsky scores of the patients in the preservative free saline flush group at sixty-day period. If the patients died during each evaluation period (5-day, 30-day and 60-day from initial intraventricular injection), their status is illustrated in figure 2 and 3 as no change in the GCS score, or zero on the Karnofsky performance status scale.

On placement of the EVD and ICP monitor, all patients received the prophylactic antibiotic, cefazoline, and if they were allergic to penicillin, vancomycin was prescribed. None of the patients developed complication of ventriculitis or arachnoiditis. In one patient, reoccurrence of bleeding was observed during the period of administration of the drug in the rtPA group and none in the preservative free saline group. This patient's systolic blood pressure was noted to increase above 180mmHg after rtPA administration, when this was observed. None of the catheters became obstructed with a clot in the rtPA group. In the preservative free saline flush group two catheters had to be replaced.

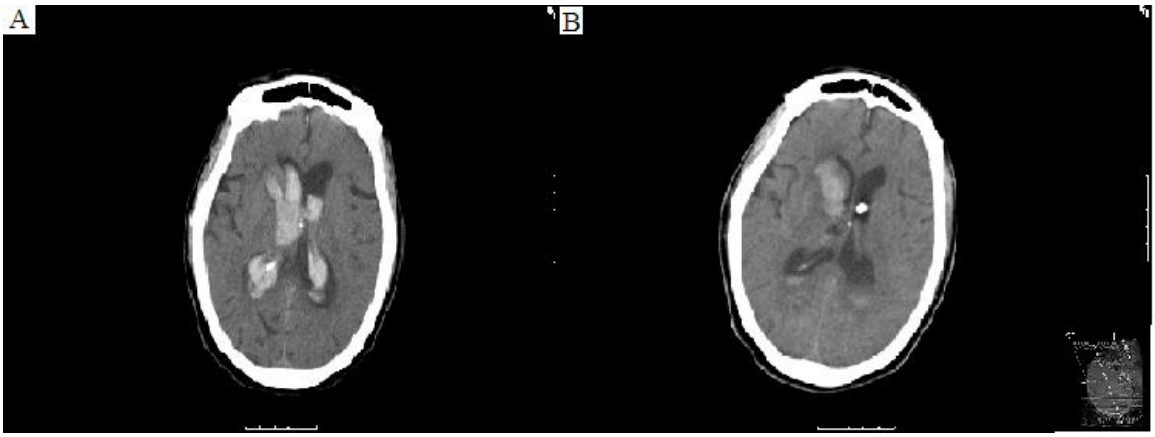

Figure 1. Initial representative CT scan from the patient group who received recombinant tissue plasminogen activator (A, Le Roux score = 14) and at end of 5-day period (B, Le Roux score = 4) showing significant resolution of the intraventricular hematoma.

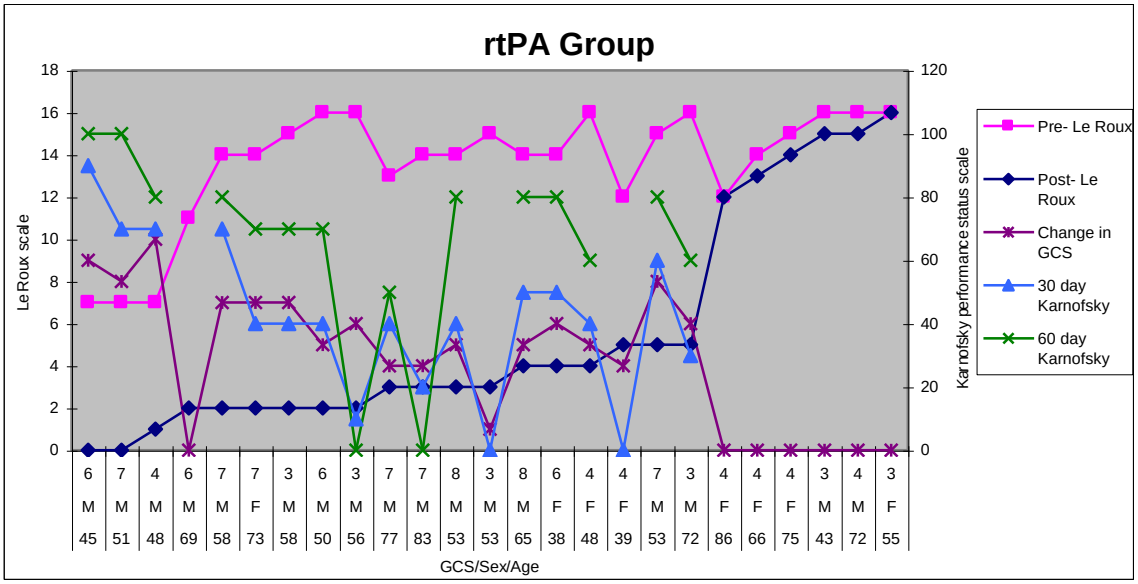

Figure 2. Patients presenting with spontaneous basal ganglia hemorrhage extending into the ventricles (measured using Le Roux grading system) received 2mg rtPA for approximately five consecutive days and clinical outcome recorded using the change in Glasgow Coma scale (GCS) at 5-day period, and Karnofsky performance status scale at 30-day and 60-day period.

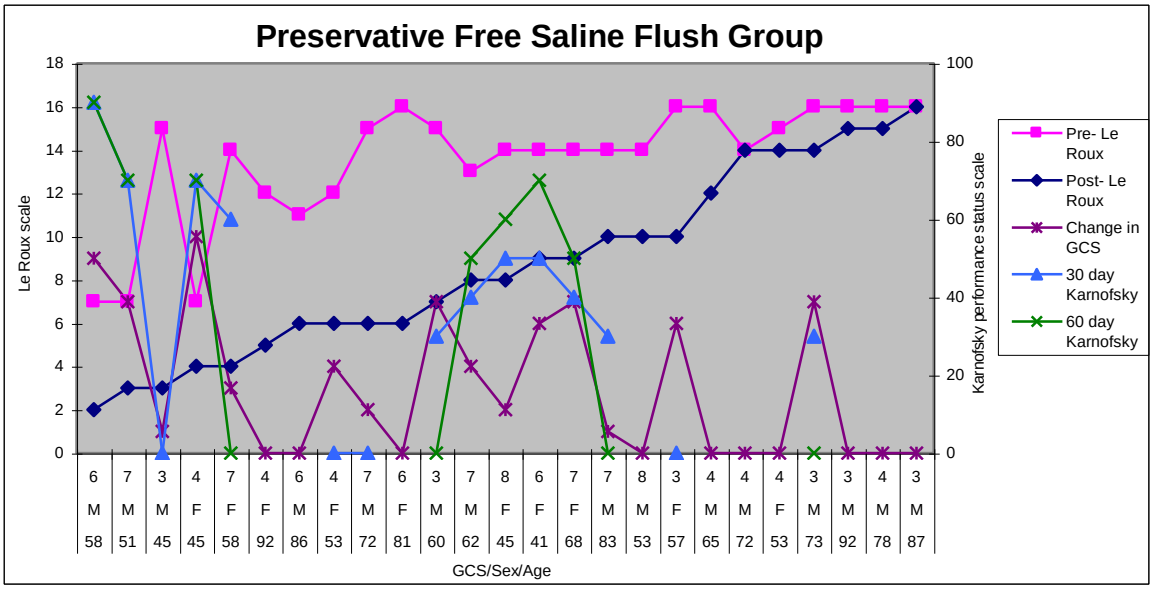

Figure 3. Patients presenting with spontaneous basal ganglia hemorrhage extending into the ventricles (measured using Le Roux grading system) received approximately 3ml of preservative free saline flush serially and clinical outcome recorded using the change in Glasgow Coma scale (GCS) at 5-day period, and Karnofsky performance status scale at 30-day and 60-day period.

DISCUSSION

The most common etiology for the IVH are hypertensive hemorrhages originating frequently from the basal ganglia extending into the ventricles.[6-8,19,22] Multiple studies have revealed that observing a decrease in density on CT scan does not mean resolution of the clot. The IVH may persist pathologically for months post-hemorrhage.[5,20,30] This may contribute to the poor prognosis we observe today.[3,16]

Multiple mechanisms have been purposed to explain the increase in morbidity with IVH involvement. IVH causes elevated intracranial pressures by obstructing the cerebral spinal flow, which in turn leads to parenchymal damage.[31] Blood products also trigger a inflammatory cascade in the ependymal and subependymal layers of the ventricular walls that further causes deleterious effects.[6,7] When intraventricular blood and CSF is inadequately drained, there is an increase in intracranial pressure and damage to ventricular walls that are detrimental to patients' prognosis.[7.10-12] Studies have shown this results in decreased cerebral blood flow, and damage to the ependymal and subependymal layers of the brain and the brain stem.[6,7,13,14] Tuhrim found clinical outcome has a strong correlation with the ventricles involved and the amount of blood present. Mayer reported IVH greater than 20ml compromises global cortical perfusion and results in severe disability or death.[13]

The goal is rapid resolution of the clot. Naff demonstrated that independent of patients age, sex, etiology of hemorrhage, EVD use, the percentage rate of radiographic clot resolution is 10.8% per day.[24] The intraventricular blood clot resolution follows first-order kinetics. They found that there is a 48-hour latency period in clot resolution and there may be clot expansion during this period. The innate CSF plasminogen/tPA thrombolytic system becomes saturated between 24 to 48 hours and then thrombolysis begins. By administering the rtPA early, the latency period is shortened and the clot resolution is initiated sooner.

Conventional treatment has been to place an EVD in attempt to evacuate the IVH which has been ineffective.[18,19,24] A number of studies have been performed involving directly introducing intraventricular thrombolytic agents to clear the ventricles. Most recent by Vereecken, an 18-patient retrospective case series showed intraventricular rtPA was effective in lysis of IVH with one patient developing ventriculities.[5] In this study, rtPA was administered in a dosage of 2mg at 12-hour intervals until CT scans showed substantial reduction. Of the eighteen patients, seven showed clinical neurological improvement, four patients died with one patient dying secondary to rtPA complication.

Findlay investigated eight patients treated with intraventricular rtPA secondary to aneurysm rupture.[21] Early aneurysm repair and lysis of IVH with rtPA facilitates rapid resolution of IVH and was found to be safe. rtPA was administered in 4mg doses at 24-hour intervals. A significant increase in CSF drainage as well decrease in ICP was noted. Clinically, six patients

had no disability, three patients had moderate disability and one patient had severe disability. No complications were reported including any hemorrhages, infectious, or catheter obstruction.

Our study shows that patients with basal ganglia hemorrhage with intraventricular extension may benefit from early intraventricular serial administration of 2mg rtPA at 24-hour intervals and EVD placement. A significant improvement in resolution of IVH is observed as well as improved morbidity and mortality rates at 30-day and 60-day period in the rtPA group compared to preservative free saline flush group. The change in GCS score between the two groups was not significant from initial to post-administration of the medications. We believe that this may due to inherent limitations of the Glasgow coma scale in evaluations of the patients' very early clinical progress. Early administration of rtPA not only improves clot resolution but also neurological outcome. Initiating early intraventricular rtPA helps shorten the innate CSF plasminogen/tPA thrombolytic system's latency period for the hemorrhage. Continuing the rtPA administration for five days, ensures constant early complete saturation of the thrombolytic system leading to clot lysis progression. Clot resolution can further improve the clinical outcome due to possible attenuation of the inflammatory cascade in the ependymal and subependymal layers of the ventricular walls that cause additional deleterious effects.[6,7]

No invasive intervention is without risks. Main risks of intraventricular administration of rtPA may include infection or increase in the hemorrhage. Hypertensive ICH with IVH is described to have high rate of rebleeding; however, our less frequent dosing of rtPA and an aggressive blood pressure management resulted in minimal adverse patient reactions. We suspect the patient who rebled was secondary to blood pressure spike.

CONCLUSION

We believe intraventricular administration of rtPA shows promising results in safely resolving IVH, maintaining patency of ventricular drainage catheter, decreasing hydrocephalus, and improving neurological outcome and mortality. With only limited number of case studies published, we believe that a large scale, double blinded, prospective, randomized, controlled study is needed to validate these results before general implementation of the rtPA for ICH with IVH.

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Purely Endoscopic Versus Traditional Open Microvascular Decompression in the Treatment of Vascular Compression Syndromes

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Purely Endoscopic Versus Traditional Open Microvascular Decompression in the Treatment of Vascular Compression Syndromes

OBJECTIVE: This retrospective paper evaluates the technique and outcomes of endoscopic vascular decompression (EVD) in patients with trigeminal neuralgia (TGN), hemifacial spasm (HFS) and cochleovestibular nerve compressive syndrome (CNCS).

METHODS: This study evaluates outcomes and length of stay in 28 patients who underwent EVD for vascular compressive disorders from 2005-2007. It also evaluates length of stay in 41 patients who underwent traditional microvascular decompression (MVD) from 1999-2004.

RESULTS: 90% (18/20) patients had resolution of their trigeminal neuralgia and 86% (6/7) had resolution of their hemifacial spasm. There were no major complications. The EVD patients had an average length of stay of 2.28 days as compared to 4.36 days for the MVD patient group. ($p< 0.001$)

CONCLUSION: EVD is a safe and effective procedure that is as successful as MVD with less morbidity and shorter hospital stays.

KEY WORDS: Trigeminal Neuralgia, Hemifacial Spasm, Tinnitus, Microvascular Decompression

INTRODUCTION

Microvascular decompression (MVD) is a well-accepted, highly successful surgical procedure for the treatment of trigeminal neuralgia (TGN) and hemifacial spasm (HFS). It also has been shown to be successful in the treatment of patients with other less common disorders such as glossopharyngeal neuralgia (GPN) and cochleovestibular nerve compressive syndrome (CNCS). MVD has historically been the most successful intervention for immediate and long-term relief of symptoms in patients with TGN and HFS.[1-4] Other interventions for the treatment of TGN include percutaneous radiofrequency rhizotomy, glycerol rhizotomy and stereotactic radiotherapy. Recently, endoscopic assisted microvascular decompression (EAMVD) has been performed to provide better intraoperative visualization of the surgical field. This technique has been a helpful adjunct in successful decompression of the affected cranial nerves. The majority of articles on this topic detail the endoscopic anatomy of the cerebellopontine angle (CPA) or use the endoscopic technique only after traditional craniotomy and vascular decompression using the

operating microscope.[6-9] Only a few articles discuss a fully endoscopic technique without the aid of an operating microscope, performed through a more limited incision and craniotomy.[10,11,12]

Endoscopes have become an integral part of skull base surgery in recent years, particularly for anterior skull based approaches. Otolaryngologists and rhinologists who have used endoscopes on a daily basis in paranasal sinus surgery have helped advance the field of minimally invasive, endoscopic skull base surgery. The experiences of endoscopic surgery for anterior skull base procedures are now encouraging the use of endoscopes for posterior fossa and lateral skull base procedures.

Some of the benefits of EVD include a smaller incision with less soft tissue mobilization, smaller craniotomy, less cerebellar retraction and panoramic visualization from lower cranial nerves to the tentorium. Endoscopes may also improve the ability to visualize areas of vascular compression not seen with the microscope, leading to a higher rate of successful outcomes.[5,8,9] Potential additional benefits of EVD include lower complication rates, shorter hospitals stays, less post-operative pain and quicker patient recovery.[11]

Despite it success, EVD does present technical challenges. Finding the exact position of the transverse-sigmoid sinus junction based on surface landmarks can be challenging and is the key to minimizing both the size of the incision and the size of the craniotomy. The lack of depth perception and 3-dimensional visualization with the endoscope creates a steep-learning curve that can significantly increase operative time until a certain level of experience is obtained. There is also additional equipment, which can increase the operating room setup time, room turnover time, and the capital expense of the new equipment required to perform this procedure.

At our institution we have performed this operation since 2005 with great success for TGN, HFS and CNCS. The purpose of this study is to discuss the technique and outcomes in a series of patients undergoing endosopic microvascular decompression (EVD).

METHODS

Since September 2005, 48 posterior fossa surgical cases have been performed at our institution using a minimally invasive, endoscopic technique via a 1.5 cm craniotomy retrosigmoid craniotomy.

This paper is a retrospective review of 28 of those patients who underwent endoscopic vascular decompression (EVD) at our institution from 2005-2007. These patients underwent EVD for TGN (20 patients), HFS (7 patients), and CNCS (1 patient). The post-operative follow-up period ranged from 3-30 months, with a mean time of 12 months. In addition to the above review, a historical retrospective review was performed looking at 41 patients who underwent traditional microvascular decompression (MVD) by the same surgeons at the same institution from 1999-2004. The hospital lengths of stay (LOS) were compared between the two study groups.

Surgical Approach

The following retrosigmoid craniotomy approach is used for all of our posterior fossa endoscopic cases, including the EVD.

Facial nerve monitoring with The NIM-response (Medtronic USA, Inc., Minneapolis, MN) and auditory brainstem response (ABR) monitoring with the cascade system (Cadwell Laboratories, Inc., Kennewick, WA) are used in all of our EVD cases.

The patient is placed in a supine position. The head is immobilized in a Mayfield head clamp to avoid any unforeseen movement of the head while the endoscope is within the cerebellopontine angle (Figure 1). The intracranial pressure is reduced by elevating the head to 30^0 administering 1 gm/Kg of Mannitol (not exceeding 75gm) followed by 20 mg of furosemide intravenously and reducing the arterial $PaCO_2$ to around 28-30 mmHg. Prior to the skin incision, the transverse-sigmoid sinus junction is approximated by connecting a line from the zygomatic root to the inion, often called the superior nuchal line. A second line approximating the posterior mastoid groove, which approximates the occipitomastoid suture line, intersects this line. A 3-4 cm oblique incision is marked and centered over the estimated craniotomy site. The 1.5 cm 'keyhole' craniotomy is placed posterior and inferior to the intersection of these two lines (Figure 2).

Traditionally, the craniotomy has been performed with a high-speed drill. Alternatively, we have recently used a 14 mm perforator with equal success. Accurate identification of the transverse-sigmoid junction is essential and the craniotomy site can be expanded using the high-speed drill or kerrison punch as necessary. A dural incision is made in the retrosigmoid dura paralleling the distal transverse and proximal sinuses regardless of the cranial nerve of interest as this provides access from the incisura and

cranial nerve IV through the foramen magnum and cranial nerve XII. A 0^0 4mm endoscope is used as the working endoscope, while the 30^0 endoscope is used only for supplemental visualization. Unlike anterior skull base procedures, the limited exposure of the CPA limits the possibility of an assistant to hold the endoscope and as such we utilize a pneumatic arm to allow the surgeon bimanual dexterity. (Figure 3) The endoscope is advance along the tentorium to the incisura and the prepontine and interpeduncular cisterns. The arachnoid is then released from these cisterns and the petrosal vein is sacrificed if necessary. At this point the endoscope is positioned over the cranial nerve of interest. The Endoscrub™ irrigation system (Medtronic, Minneapolis, MN) is used to maintain clear visualization as well as continuously cool the heat emitted from the xenon light source. A 360^0 inspection of the cranial nerve is performed at the root entry zone. The vascular decompression is performed by placing a small piece of Teflon felt between the offending vessel and nerve at the root entry zone (Figure 4). Prior to closure, any exposed mastoid air cells are obliterated with bone wax. The dura is closed in a watertight fashion and the craniectomy site reconstructed with hydroxyapatite. A head dressing is used for 2 days to apply pressure to the surgical site.

RESULTS

The postoperative results for EVD for TGN showed complete relief of preoperative facial pain symptoms in 18/20 (90%) cases. The 2 patients without complete relief have had at least partial relief in symptoms. Those 2 patients also have the shortest follow-up period of only 3 months. There was one minor complication of a wound dehiscence that required debridement and closure in the operating room 1 month after surgery. This was attributed to the hydroxyapatite paste seeping into the soft tissues prior to complete hardening. None of the patients had hearing loss based on intraoperative ABR monitoring and postoperative symptoms. There were no other postoperative complications, including, dizziness, facial weakness or CSF leak.

The postoperative results for EVD for HFS were complete resolution of symptoms in 6/7 (86%) patients with 1 patient having recurrence of facial spasms 9 months after initial success. That patient has had subsequent re-exploration and a second vascular loop of PICA was found. This patient is now symptom-free. Complications included transient facial nerve weakness in 1 patient. This patient was a grade 2/6 on the House-Brackmann facial nerve grading scale in the immediate postoperative period, which

returned to normal after 1 month. All patients had some degree of post-operative dizziness that resolved in all cases after a short period of days to weeks. One out of five patients did show a mild sensorineural hearing loss in the mid-frequencies and had a decrease in their speech reception threshold from 0 dB to 15 dB. The speech discrimination score was unchaned at 100%.

The 1 patient who underwent EVD for cochleovestibular compressive syndrome (CNCS) had a slow, steady resolution in her symptoms over a 2-month period and is now symptom free.

The calculated average LOS for the 14 patients undergoing EVD for TGN was 2.28 days. These results were compared to historical data on the 41 patients undergoing traditional MVD for TGN. The average LOS for these 41 patients was 4.39 days. The data was analyzed using a student T-test and the results showed that there was a statistically significant difference in the LOS between these two patient groups. ($p = < 0.001$).

DISCUSSION

The traditional microvascular decompression (MVD) using the operating microscope for surgical treatment of compressive syndromes is a well-accepted curative treatment for patients with trigeminal neuralgia (TGN) and hemifacial spasm (HFS). Several large series of TGN patients undergoing MVD have shown a 82-100% rate for complete relief of symptoms. These results decrease slightly to 75-90% for three-year follow-up data.[1,2,13,14] Barker et al. published a landmark article of 1185 patients undergoing MVD for TGN. Their initial success was 94-97%, which decreased to 70% for those patients that were followed for ten years.[2] Data for endoscopic vascular decompression (EVD) has only recently been reported in one article by Kabil et al. in 2005. EVD was performed on 255 patients with a 95% complete success rate. This decreased to 93% at three-years follow-up.[11]

Moffat et al. did a review of several major studies reporting the success rates for MVD in HFS patients. The success rates of symptom-free patients ranged from 79%-97%.[7] There is evidence that with long-term follow-up success declines as patients develop recurrences. Long-term follow-up studies show recurrence rates ranging from 1-13%.[5,6,8,15]

For the past decade or more successful surgeons have been using the endoscope in posterior fossa procedures as an adjunct to the operating microscope showing several benefits. These procedures are often

referred to as endoscopic-assisted microvacular decompression (EAMVD). Several recent papers, all from the same institution, have pioneered a fully endoscopic technique referred to as endoscopic vascular decompression (EVD).[10,11,12]

Identification of the approximate location of the junction of the transverse and sigmoid sinuses is the first critical step in performing EVD. Inaccuracy will lead to a larger incision, greater soft tissue dissection and a larger craniotomy. We use two lines, the superior nuchal line and the posterior mastoid groove (occipito-mastoid suture) as our surface landmarks for the transverse-sigmoid sinus junction. The superior limit of our craniotomy will be the intersection of these two lines and our skin incision will be centered obliquely over our planned craniotomy site. The superior nuchal line, which is a line drawn from the zygomatic root to the inion, has been shown to very accurately correspond to the rostrocaudal location of the transverse sinus.[16]

Some authors have used a similar technique with their two lines being a posterior extension of the Frankfurt horizontal line and the posterior margin of the mastoid.[6] The Frankfurt line is a line joining the lowest point of the inferior orbital rim with the superior border of the external auditory meatus. The Frankfurt line is traditionally used in the cosmetic and reconstructive surgery literature to accurately compare surgical results. When this line is extended posteriorly, it seems to less accurately define the location of the transverse sinus than the superior nuchal line.[16] The asterion has been thought to be another key cranial surface landmark for identifying the transverse-sigmoid junction. It was evaluated by Day and Tschabitscher on 100 anatomic specimens, and they proved that the asterion can be less reliable than previously thought. They found that is was located over the transverse or sigmoid sinus complex in only 66% of left and 61% of right specimens.[17] Another drawback of the asterion is that its location cannot accurately be determined through the skin and soft tissue. This can make exposure challenging when trying to limit skin incisions to 3-4 cm in length.

The first published account of a fully endoscopic posterior fossa procedure was a paper by Eby and Shahinian reporting on 3 patients who underwent EVD for HFS.[10] Since that first report in 2001, Shahinian has published multiple studies evaluating his results of endoscopic surgery for HFS, TGN, GPN and removal of cerebellopontine angle (CPA) masses. Prior to these reports the endoscope had been used only as an investigational tool or as an adjunct to the operating microscope. One of the first studies

evaluating the potential for endoscopy was performed in 1993 by O'Donoghue and Flynn; they found that endoscopy of the posterior fossa was feasible and provided adequate visualization from the tentorium to the lower cranial nerves. A major drawback that they and other more recent authors have commented on is the poor depth perception compared to binocular vision with the operating microscope.[7,9] Lack of depth perception can be problematic, but with proper technique, instrumentation and experience this can be overcome without compromising patient safety.

Magnan et al. reported one of the first series on endoscopic-assisted surgery of the posterior fossa in 43 patients. They reported that the main purpose of endoscopy is to accurately find the vessel responsible for the compressive syndrome. The culprit vessel will more likely be found with the minimally invasive technique as limited cerebellar retraction will preserve the neurovascular relationships.[8] The ability to more often identify the offending vessel(s) will improve surgical outcomes. [7]

One of the major drawbacks to MVD is the risk of a negative exploration. Despite recent advances, there still is no radiological imaging that can identify vascular compression with any degree of certainty. Even in the largest studies by experienced surgeons, there is at least a 1-2% negative exploration rate.[18] A negative exploration can mean either a misdiagnosis or failure to locate the compressive vessel. Teo in 2006 reported that 33% of his cases of arterial compression were poorly seen (25%) or missed (8%) by the operating microscope. Endoscopic surgery can provide surgeons the ability to more often identify the offending vessel(s), therefore improve surgical outcomes. [5]

There are a few reported limitations to endoscopic surgery that need to be addressed to safely perform the EVD procedure. Most endoscopic-assisted MVD procedures have been performed by the surgeon holding the endoscope in one hand, thereby, preventing bimanual dexterity. The positioning of the patient and equipment for these procedures does not comfortably allow an assistance to safely hold the camera. The introduction of a poly-articulated pneumatic arm that can hold the endoscope securely in the CPA has made EVD possible. Another problem reported, can be poor visualization due to blood, CSF or condensation.[19] We use an endoscopic irrigator (Endoscrub^{tm}– Medtronic USA, Inc., Minneapolis, MN) and have not found this to be a major problem.

The incidence of complications from MVD, EAMVD and EVD are all low. For trigeminal neuralgia patients undergoing decompression, the most common complications are facial nerve weakness

and facial numbness. Rare complications include CSF leak and hearing loss. In our study no patients had significant complaints of facial numbness and there were no cases of facial weakness, CSF leak or hearing loss. Shahinian compared his complications from EVD to several large series of MVD patients. For his 255 patients undergoing EVD for TGN there was a 0.8 % incidence of temporary facial weakness and no cases of permanent paresis or paralysis. For MVD patients the incidence for temporary facial weakness ranged from 0.5 – 9.5 %. The incidence of temporary and mild, permanent facial numbness was comparable between the EVD and MVD groups. The incidence of hearing loss was < 1% for EVD patients. Historical MVD series give an incidence of profound hearing loss ranging from 1.2 – 5.5 %. The vestibulocochlear nerve can be sensitive to manipulation and a profound unilateral hearing loss is a significant postoperative comorbidity that can significantly affect a patient's quality of life. With a small craniotomy and much less cerebellar retraction, EVD appears to have significantly less risk of hearing loss than MVD.[15,18]

For patients undergoing EVD for HFS, the risks of facial nerve weakness, temporary or permanent are greater because the seventh and eighth nerve complex must be manipulated to relieve the vascular compression. Dizziness was a universal postoperative symptom in all of our patients that resolved over days to weeks. One patient had a mild transient facial weakness and one patient had a mild, but noticeable decline in his audiogram. In reviewing several large series of HFS patients undergoing MVD the incidence of sensorineural hearing loss ranged from 5 – 20%. The incidence of transient facial palsy also varied between 2.7 – 18%.[6,8,14,20] In four studies with a combined total number of 252 patients, only one patient was reported to have a permanent facial paralysis.

CONCLUSION

We conclude that endoscopic vascular decompression (EVD) without the aid of the operating microscope is a safe and effective procedure for the treatment of patients with trigeminal neuralgia, hemifacial spasm and the other less common compressive syndromes such as glossopharyngeal neuralgia and vestibulocochlear compressive syndrome. The fully endoscopic technique has its challenges that can be overcome with the proper training, equipment and experience. Outcomes have been shown by our study as well as other EVD studies to be similar or in some cases better than the standards set forth by traditional

MVD studies. In addition to comparable results with the traditional microscopic technique, endoscopy provides added benefits that are significant. EVD is a less invasive procedure with smaller incisions, smaller craniotomies and shorter hospital stays, leading to less patient morbidity and improved quality of life.

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FIGURES

Figure 1: Operating room set-up and patient position.

Figure 2: A 1.4 cm retrosigmoid craniotomy.

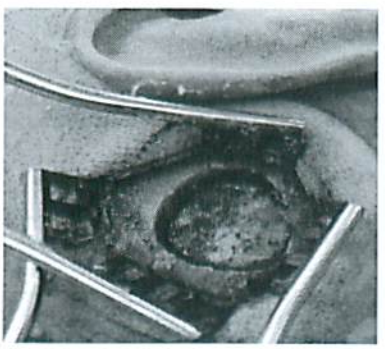


Figure 3: Pneumatic arm holding camera, video monitor and operating surgeon view.

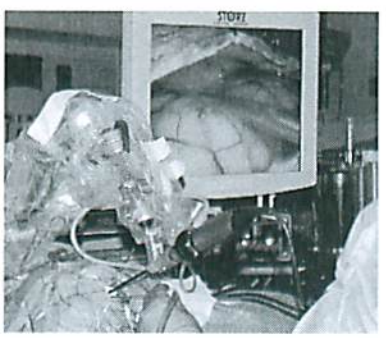
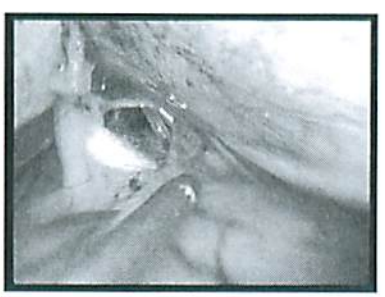


Figure 4: Endoscopic view of vascular decompression of trigeminal nerve root entry zone.



Aneurysm Clips for Durotomy Repair: A Technical Note

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Abstract

Objective

Dural injury is a common complication of lumbar spine surgery. Primary closure is the gold standard. This technical note describes a failed primary closure of a durotomy revised utilizing an aneurysm clip.

Methods

From 2005-2009, five patients underwent repair of a durotomy utilizing aneurysm clips. Resolution of the CSF leak was seen in all patients. To illustrate, an 84 y/o woman underwent a laminectomy with an inadvertent dural tear that was primarily repaired with suture. On postoperative day eight, the patient presented with new incisional drainage. The wound was explored and the dura had torn around the previous sutured closure. A curved aneurysm clip was used to obtain dural closure. Postoperatively the patient's incision remained dry.

Results

Microsurgical closure with suture has been the primary modality in durotomy repair. Difficulty arises when the dura is friable, micro-tears are present and suturing worsens the durotomy. As well, many times the durotomy is caused along a bony edge with limited visualization, requiring additional bone removal to suture, risking destabilization of the spine.

Conclusion

This technical note describes the application of an aneurysm clip to treat a recurrent durotomy where the standard practice of sutured closure failed. Aneurysm clips offer a quick, safe and secure manner to close dura without risking spinal destabilization. They offer significant benefit to already torn, friable dura. Postoperatively, patients have no limitations therefore are prevented from being exposed to additional risks associated with bedrest. Therefore, aneurysm clips are cost and clinically effective in the management of dural injuries.

Key Words: aneurysm clips, cerebrospinal fluid leak, durotomy

Introduction

Dural injury is an unfortunate complication of lumbar spine surgery. The incidence varies from 1-17%[1]. The neurologic sequelae range from remaining asymptomatic to meningitis with prolonged hospital stay, pseudomeningocele, cerebrospinal fluid (CSF) fistula, and nerve root herniation and injury. The primary goal is prevention, however iatrogenic injuries do occur and happen more often with older patients lending to thinner dura, prolonged stenosis, atrophic ligamentum flavum, and revision surgery with scar tissue. Treatment of dural injuries is varied; however primary closure is the gold standard. Aneurysms clips have not been previously described to treat dural injuries; this technical note describes a case series of durotomies treated successfully with aneurysm clips.

Material and Methods

From 2005-2009, five patients have been treated at Providence Hospital and Medical Center utilizing aneurysm clips for durotomy closure. All the patients were female with an age range from 31- 89. Two patients had a microdiscectomy complicated by a durotomy, two patients had a lumbar laminectomy, and the other durotomy was after sectioning the T2 nerve root during epidural tumor resection. One patient underwent an unsuccessful epidural blood patch for treatment of spinal headaches prior to wound exploration. Aneurysm clips were used in all of the above procedures with resolution of CSF leak, with only one patient returning to the operating room for repositioning of the clip due to improper application of aneurysm clip (the clip was placed over suture, thereby reducing the effective force on the dura itself). The following is a case presentation of a durotomy incurred after a lumbar laminectomy.

An 84 y/o woman underwent lumbar decompressive laminectomy L4-5 for spinal stenosis. The procedure was complicated by dural tear that was primarily repaired with 6-0 Prolene suture in a purse string fashion. After the dural repair, no cerebrospinal fluid was noted to be leaking. Postoperative day four, patient was noted to have small amount of serosanginous fluid egressing from her lumbar wound. Clinically she was doing well, afebrile, without headache and planned for discharge. The wound was oversewn and remained dry. On postoperative day eight the patient presented with new drainage from her wound. A magnetic resonance imaging (MRI) scan was obtained and patient was noted to have a pseudomeningocele. The patient returned to the operating room where the wound was explored. The durotomy was encountered and it was noted that the dura had torn around the previous sutured closure. At this time a curved aneurysm clip was used to obtain dural closure. The dural tear was isolated away from the nerve roots. The aneurysm clip was opened and placed around the durotomy site. No nervous tissue was present between the clip tips (Figures 1-3). A sustained Valsalva of 40 mmHg was maintained for 15 seconds without any CSF egress or any dislodgment of the clip. As the dura was inspected, no other durotomies were found and the wound remained dry. The wound was then closed in layered fashion. Postoperatively the patient's incision remained dry and patient was transferred to rehabilitation.

Results

From 2005- 2009, five patients have been successfully treated with aneurysm clips for dural injury. No patient experienced complications from the aneurysm clip application or use. One patient did return to the operating room for clip repositioning. As to date, no patient has represented with a CSF leak or spinal headache. Imaging studies have been obtained without evidence of significant artifact (Figures 4, 5 and 6).

Discussion

Although prevention is the goal in adverting durotomies, the unintended dural injury is a complication of lumbar spine surgery. There are several factors that preclude a higher risk: age, revision surgery, radiation, instrumentation, and prolonged stenosis[2].

The management of dural injuries is dependent on a multitude of factors. Yet the main goal is the same, bringing the edges of the dura together so the injury can heal. If the injury is noted intraoperatively, primary closure is preferred. However this is also dependent on the location of the durotomy and if a single tear or many micro-tears are present. Microsurgical closure with suture has been the primary modality in durotomy repair. Various glues have been used to assist in closure as well as incorporation of muscle into the dural rent. Moreover, several suturing techniques exist from simple sutures to a patch graft to a lateral patch technique[2]. Difficulty arises when the dura is friable, micro-tears are present and suturing worsens the durotomy. As well, many times the durotomy is caused along a bony edge with limited visualization. In order to close the tear, more often than not, extra bone must be removed to facilitate microsurgical closure. The most feared complication to extra bone removal is destabilization of the spine. This is where the aneurysm clip is superior to a suture closure. Friable dura and micro-tears are easily handled with one or two aneurysm clips. Intraoperatively CSF is suctioned to allow dural edges to come together and the clip is applied. As well, there is no extra bone removal as a right-angled aneurysm clip can be used easily along the bony edges.

Postoperatively, patients with known durotomy or patients with pseudomeningocele or CSF fistula are managed in a variety of ways. Typically bedrest is advocated with pseudomeningoceles, whereas CSF fistulas undergo oversewing of the wound then bedrest[3, 4]. This raises several issues. First it is the active leaking of CSF that causes the spinal, intracranial hypotension headache. Therefore early repair should be advocated. Secondly, bedrest places the patient at risk for medical complications such as deep vein thrombosis [5], urinary tract infection [6] and physical decompensation. These risks are alleviated with early ambulation. Thirdly, there is the additional cost of a longer hospital stay. On review of the 2007 national statistics of charges from the Healthcare Cost and Utilization Project for spondylosis, the mean and median charges were $40,762 and $26,665 for mean and median length-of-stay (LOS) of three and two days respectively. This averages to a mean and median charge per day of $13,587 and $13,333[7]. Closed subarachnoid drainage for up to seven days has also been advocated in

management of CSF fistulas and pseudomeningoceles [2-4]. Again, similar risks seen with bedrest apply, along with the added risk of meningitis, spinal headaches, wound infection and nerve root irritation. There are also a few articles that discuss the use of an epidural blood patch[2-4, 8, 9]. However this is usually requires additional bed rest [9] occasionally along with LD drainage[10], prolonging the hospital stay or the active CSF leak can continue for several days post epidural patch[8], increasing the risk of meningitis.

There are a few articles that address dural closure with clips. Ferroli et al describe the use of self-closing nitinol clips for a recurrent durotomy[11]. The trouble with the U-clip is it is a penetrating clip, therefore creates holes in already fragile dura. As well, the U-clip has been reported to be difficult to remove[12]. Levy et al performed a study on cadaveric durotomies utilizing hemostatic vascular clips, a designed titatnium clip (similar to an aneurysm clip), and suture. They found that the titanium clip withstood the pressures comparable to the hemostatic clip and suture. However the clips were faster to apply and the titanium clips were easier to control and did not lacerate the tissue[13]. Timothy et al explored using non-penetrating vascular clips for dural closure for planned surgical durotomies. They also comment on the disadvantages of the vascular clips, including inability to reposition or reuse the clips[14]. The benefits of aneurysm clips for primary or recurrent durotomy are numerous.

Intraoperatively they provide a quick, reliable closure that doesn't require extra bone removal, thereby not compromising stability. They are easily removed and reapplied should initial placement be incorrect. They are able to undergo intraoperative testing, such as Valsalva without dislodgement. Postoperatively, the patients are ambulatory and discharged in a typical manner. There are no restrictions placed on the patient, thereby reducing the risk of deep vein thrombosis that is seen with recumbency. Should imaging be required, there is minimal artifact noted on MRI that does not preclude the reading of the study, which Timothy et al concur[14]. Although artifact is increased in a 3.0-T MRI, artifact areas can be reduced by manipulating the imaging parameters, resulting in similar artifact areas seen on a 1.5-T MRI[15].

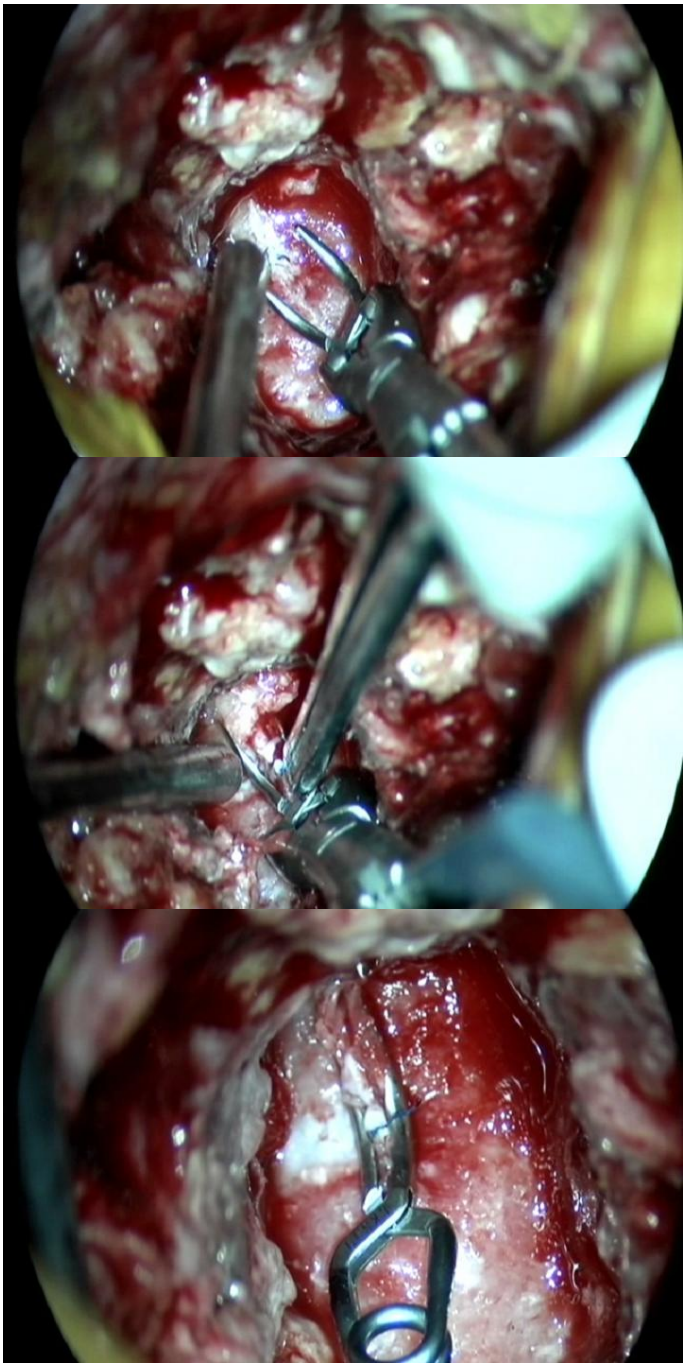
In cost analysis in regards to aneurysm clip use for primary or recurrent durotomy repair, several cost saving benefits are noticed. As described above, the length of stay is not increased; therefore the amount saved in comparison to a 3-7 day longer hospital stay with bedrest is substantial, with an average cost per day of $13,000[7]. As well, the cost of lumbar drainage alone is comparable to an aneurysm clip ($270-300), without consideration of additional cost of longer hospital stay. One article states that bedrest is not mandatory after an incidental durotomy treated with dural stitches and fibrin glue[16]. Of note, the commonly used fibrin glue (Tisseel ® Baxter or Evicel ® Johnson and Johnson) costs approximately $200-400, as well has a low risk of transmitting infectious agents such as viruses and Creutzfeld-Jakob disease (CJD) agent. Therefore, aneurysms clips are cost effective manner to treat dural tears.

The technique presented in this article represents a quick, secure, and definitive closure for dural injuries. With the additional benefit of using a standard aneurysm clip, which is readily available at most institutions, as well as it not being cost prohibitive as many proprietary clips are. As illustrated in the case report, the aneurysm clip succeeded where traditional suture repair failed. The reason for failure is indeterminate; however atrophic dura most likely played a part. As demonstrated by other authors, titanium clips endure well in thinned dura, therefore perhaps aneurysm clips should be utilized in primary closure where thinned dura is encountered[13].

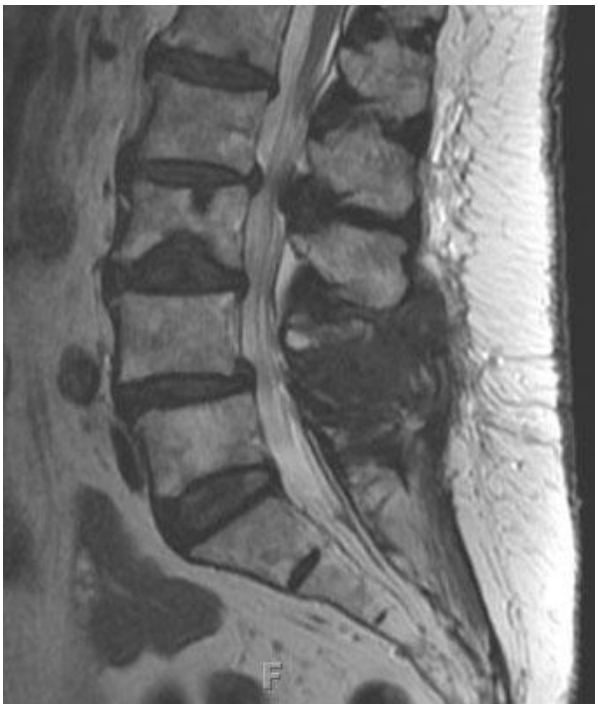
Conclusion

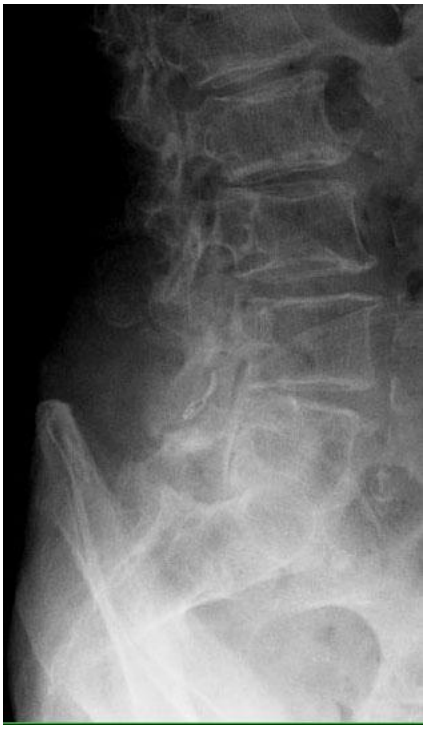
This technical note describes application of an aneurysm clip to treat a recurrent durotomy where the standard practice of sutured closure failed. Aneurysm clips offer a quick, safe and secure manner to close dura without risking destabilization of the spine. They offer significant benefit to already torn, friable dura. Postoperatively, the patient has no limitations therefore are prevented from being exposed to additional risks associated with bedrest. Therefore, aneurysm clips are cost and clinically effective in the management of dural injuries.

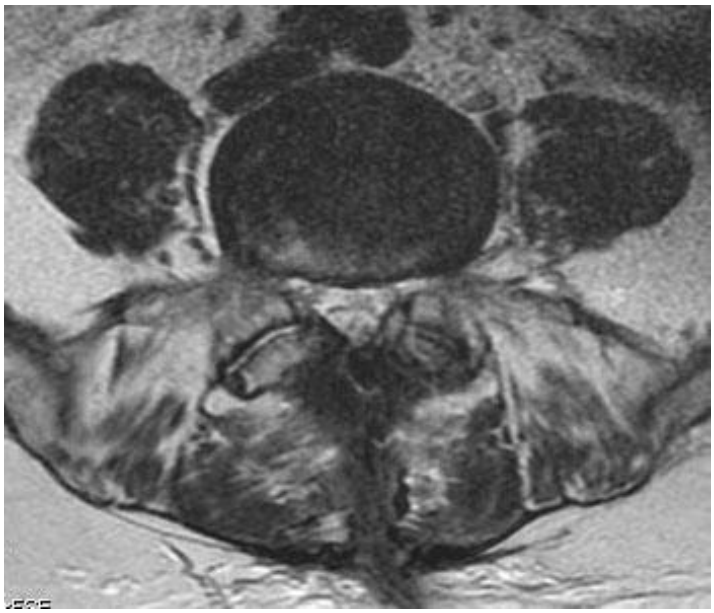
Figures 1, 2, 3- Application of aneurysm clip to durotomy



Figures 4, 5, and 6: Lumbar T2 MRI, Lateral X-ray, and Axial T2 MRI







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Sagittal Correction from a Posterior Approach Combining the Smith-Peterson Osteotomy, Release of the ALL, and Placement of a Large, Extreme Anterior Cage

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Abstract

Introduction: Adult degenerative flat back or lumbar degenerative kyphosis leads to muscle fatigue and intractable back pain. This is a surgical condition that can be treated using operations aimed at correcting the sagittal balance. The Smith-Peterson Osteotomy (SPO) technique can provide a mean of 10 degrees of lordosis per level. A pedicle subtraction osteotomy (PSO) provides up to 40 degrees of lordosis per level, but is fraught with up to 50% surgical morbidity rates. We present a technique that combines the Smith-Peterson osteotomy with release of the anterior longitudinal ligament (ALL) and placement of a large, extreme-anterior cage via a traditional TLIF approach.

Methods:

We conducted a retrospective review of 16 patients who had lumbar or thoracolumbar degenerative kyphosis. Each patient underwent a spinal fusion that included a traditional Smith-Peterson osteotomy. A TLIF approach was used to perform an interbody fusion and the anterior longitudinal ligament was disconnected. This maneuver allowed for insertion of an expandable or large cage placed extremely anterior through the ALL. The pedicle screws were subsequently compressed to provide lordosis and correct the degenerative kyphosis.

Results:

Sixteen patients mean age of 71 (range 51-83) were included. Review of pre- and post-operative radiographs reveal a correction of up to 30-45 degrees of lumbar lordosis per level. There were no intraoperative complications and no major morbidities or mortalities

Conclusion:

A Smith-Peterson osteotomy combined with release of the ALL and placement of a large anterior cage via a TLIF approach is a safe and effective treatment of degenerative lumbar kyphosis in patients requiring significant correction of kyphosis

KEYWORDS Adult degenerative scoliosis, flat-back syndrome, sagittal balance, Smith-Petersen osteotomy, pedicle subtraction osteotomy

Introduction

Adult spinal deformity, and particularly sagittal imbalance, is a problem that poses great challenges to spinal surgeons. Patients with "flat-back syndrome" have a loss of normal lumbar lordosis combined with forward inclination of the trunk, and inability to stand erect without knee flexion and pain. [i] Patients compensate with extension of the hips as well as knee flexion and cervical extension to maintain horizontal gaze; the strain of trying to achieve erect posture causes fatigue and severe pain.

Correcting sagittal deformities relies on osteotomies to create enough flexibility to correct the deformity. Previous techniques have been described. In 1945, Smith-Petersen et al. described a technique involving bilateral facetectomies bone removal for surgical correction of deformity associated with ankylosing spondylitis. [ii] The indications for SPO have gradually been expanded to include the treatment of other types of kyphotic deformities or the lumbar and thoracic spine.

Because the traditional SPO can only achieve 10 degrees per level,[iii] multi-level SPOs must be performed to achieve the necessary amount of correction needed in many patients. This leads to increased blood loss, longer operative time, and ultimately, high rates of morbidity. Pedicle subtraction osteotomy (PSO) has also been described and can achieve greater extension but is also reported to be associated with significant perioperative morbidity. [iv,v]

We present a method in which we performed an SPO combined with release of the anterior longitudinal ligament and extreme anterior cage placement via a traditional transforaminal interbody technique to achieve greater correction of the kyphotic deformity.

Patients and Methods

We conducted a retrospective study of patients with flat back syndrome and sagittal imbalance. All patients were treated by a single surgeon between October 2007 and February 2009. All patients were ambulatory preoperatively and presented with a primary complaint of severe low back pain as well as an inability to ambulate for long distances. We identified a 16-patient cohort (mean age, 71 yr; range, range, 51-83 yr). Five patients underwent SPO with Extreme Anterior Cage placement at L1-2, eight at L2-3, and three at L3-4. Ten patients had previously undergone at least one spine surgery. Eleven patients had preoperative comorbidities that increased their surgical risk stratification (i.e., asthma, diabetes, cancer).

Patient	Age	Sex	Comorbidities	Previous Sx	Indication	No. Posterior levels fused	Level of PSO-EAC

1	81	M	Yes	Yes	Acquired Flat Back Syndrome	4	L1-2
2	51	M	Yes	No	Adult Degenerative Scoliosis	3	L3-4
3	68	M	No	Yes	Adult Degenerative Scoliosis	2	L2-3
4	58	F	No	No	Adult Degenerative Scoliosis	3	L2-3
5	67	F	Yes	Yes	Adult Degenerative Scoliosis	3	L1-2
6	62	F	Yes	Yes	Acquired Flat Back Syndrome	6	L3-4
7	74	M	Yes	No	Adult Degenerative Scoliosis	8	L#-4
8	73	F	No	Yes	Acquired Flat Back Syndrome	12	L1-2
9	78	M	Yes	Yes	Adult Degenerative Scoliosis	9	L2-3
10	48	M	No	No	Adult Degenerative Scoliosis	4	L2-3
11	75	F	No	Yes	Acquired Flat Back Syndrome	4	L1-2
12	81	F	Yes	Yes	Adult Degenerative Scoliosis	3	L2-3
13	80	F	Yes	No	Adult Degenerative Scoliosis	5	L2-3
14	73	M	Yes	Yes	Adult Degenerative Scoliosis	2	L!-2
15	82	M	Yes	No	Adult Degenerative Scoliosis	5	L2-3
16	81	M	Yes	Yes	Adult Degenerative Scoliosis	2	L2-3

Operative Technique

Positioning

All patients were positioned prone on an open-frame, radiolucent operating table. The open frame allows the patient's abdomen to float freely, allowing gravity to assist in the creation of lumbar lordosis. We feel the open-frame table is a necessity when attempting to restore lumbar lordosis.

Neurophysiological Monitoring

Somatosensory evoked potentials, free running electromyography (EMG) of the lower extremities as well as evoked EMGs with pedicle screw stimulation were all utilized in each surgery. For prolonged cases in the prone position, we also conduct neurophysiological monitoring of the upper extremities to monitor for brachial plexus tension or injury and to serve as a control for comparison with lower-extremity neuromonitoring. These techniques have been proven to be valuable in previous reports.[vi]

Anesthetic Considerations

The anesthesiologists avoid the use of medications that can blunt MEP, somatosensory evoked potentials, and EMG signals. An arterial line as well as multiple large-lumen peripheral IV's were placed to allow for blood pressure monitoring and volume resuscitation during surgery. We also routinely use an intraoperative cell-saver to decrease the need for blood transfusions. For cases involving blood loss in excess of 2L, patients often need not only a transfusion of packed red blood cells but also fresh-frozen plasma to replace coagulation factors. Fresh-frozen plasma should transfused prophylactically based upon blood loss rather than in response to laboratory evidence of increased prothrombin time. [vii]

Surgical Technique

Exposure of the spine was performed in the traditional manner, exposing only the levels necessary. Care was taken to avoid using unipolar bovie near the facet capsule of the most superior level, which we believe can reduce the incidence of adjacent level disease by not disrupting the neurovascular supply to the facet.

Subsequently, pedicle screws were placed at the levels adjacent to the osteotomy. Many of the patients in our study had significant degenerative disc disease and kyphoscoliosis so long constructs were necessary. We routinely performed pedicle screw EMG stimulation to verify correct placement of pedicle screws. At the level of the osteotomy, a laminectomy and bilateral complete facetectomy was performed. A small ridge of bone along the superior lamina was left in place, which provides a fulcrum against which a laminar spreader is used to distract the disc space. We then remove the ligamentum flavum at that level or, in revision cases, all scar tissue is carefully removed to exposed the dura.

At the level of the osteotomy, a traditional transforaminal approach is used to complete the discectomy. We typically approach the disc from the side with the most neural compression to ensure complete decompression of the nerve. A complete and radical discectomy must be performed, removing the entire disc. In cases that are difficult to remove the entire disc, we will approach the disc from both sides. When the discectomy is complete, a series of disc space distractors are used to carefully pierce the anterior longitudinal ligament. This ligament must be disconnected along the entire anterior aspect of the vertebral body to allow enough flexibility to achieve the desired amount of lordosis. The disc space distractors that we use are blunt to lessen the risk of injury to structures anterior to the ALL. A small up-going curette can also be used to

scrap along the ALL if necessary. We then place a PEEK cage. Because of the large size, the insertion of the cage can be very difficult and care must be taken to avoid nerve injury. Therefore, the cage is typically inserted sideways and twisted 90 degrees when it is in the appropriate place. The goal is to place the cage half in the disc space and half anterior to the ALL. This provides an anterior fulcrum against which to provided extension and lordosis at that level. If there is a large anterior osteophyte, it must be broken with osteotomes to ensure that there is complete disconnection of the anterior column.

After the cage is inserted, bone graft and any synthetic fusion materials are placed. We typically used bone morphogenic protein. The laminar spreader is removed, releasing the distraction very slowly. The position of the cage is verified using fluoroscopy. We then re-explore each foramina to ensure complete decompression of the exiting nerve root. Because the posterior column of the spine is being shortened the nerve roots must be explored after placement of the cage.

We then complete a traditional postero-lateral decortication and fusion. The remainder of the surgery proceeds with other levels of interbody fusion, if necessary. This is followed by placement of the rod and closure of the wound.

RESULTS

The mean follow-up period for clinical and radiographic outcome variables was 12 months (range 18-3 months). The mean intraoperative blood loss was 579 mLs. The mean operative duration was four hours and twenty minutes. The mean preoperative lumbar lordosis was 9.6 degrees before surgery and increased to 39.4 degrees at follow-up.

The mean Numeric Rating Scale for pain score improved from 8.3 (back pain) and 7.9 (leg pain) before surgery to 3.3 (back pain) and 1.5 (leg pain) postoperatively. The Numeric Rating Scale was only completed on those patients who had at least 6 months of post-operative follow-up.

The amount of correction at the level of the osteotomy was also calculated. The lumbar lordosis was a mean of -4.9 degrees pre-operatively had improved to a mean of 21.8 degrees postoperatively. The mean change in lordosis was 26.7 degrees (range 12.6 - 45.9 degrees). The C7 plum line, measured from the mid-body of C7 to the anterior-superior aspect of the S1 promontory was an average of 4.4 cm (range 3.0-5.1cm) anterior to the S1 promontory pre-operatively. Postoperative plum line was a mean of -0.3cm (range -2cm-1.1cm).

Patients who had at least 6 months of follow-up were evaluated for completed fusion. There were no cases of pseudoarthrosis and no cases of angular motion revealed by dynamic radiography. There were no cases of infection or neural injury in any case. There were no cases of vascular injury. Three cases had post-operative ileuses that lengthened their hospital stay. Two patients had DVT's despite early prophylaxis with subcutaneous low-dose heparin, which we typically begin on post-operative day number one.

Pre and post-operative CT scans of two patients can be view in Figure 1 and Figure 2.

DISCUSSION

Sagittal plane imbalance is very debilitating for patients; it results in significant back pain, limitation in mobility, and a poor quality of life. [viii, ix] The sagittal-vertical axis is determined and defined by a plumb line from the mid-C7 vertebral body on a lateral x-ray in the standing position. Previous studies have described a "normal" sagittal balance when the plumb line passes 2 cm to 4 cm posterior to the ventral S1 vertebra or 1 cm posterior to the L5-S1 disk space. All of our patients were out of sagittal balance pre-operatively and were corrected to within 2-4 cm posterior to the S1 promontory.

Previous techniques that have been described to correct sagittal imbalance include the Smith-Petersen Osteotomy (SPO) and the Pedicle Subtraction Osteotomy (PSO). Using a variety of statistical analyses, Cho et al. prospectively compared Smith-Petersen osteotomies with pedicle subtraction osteotomies for the treatment of imbalances in the sagittal plane of the spine in seventy-one patients. [x] In their study, the SPO achieved an average overall correction of 10.7 degrees per segment. The group treated with a pedicle subtraction osteotomy had an average correction of 31.7 degrees. We present a method that can achieve a similar amount of correction per level without the associated blood loss and risk to neural elements as is seen in a PSO. PSO's are technically demanding and involve substantial mobilization of the dura, as well as substantial blood loss. [xi] Buchowski et al. reported the prevalence of intraoperative and postoperative neurologic deficits to be 11.1% and the prevalence of permanent deficits to be 2.8% in a study of 109 patients who had undergone a PSO. [xii] In our study we have had no patients with transient or permanent neurologic deficits.

A Smith-Petersen osteotomy, like our technique, shortens the posterior column. There is a natural concern that our technique could result in injury of the major vessels, particularly the abdominal aorta. However, we have had no cases of vascular injury. There have also been reports of complications such as intraspinal hematoma and intestinal obstruction or superior mesenteric artery syndrome extreme sagittal plan correction. [xiii, xiv] We did not see any similar complications in our series.

We present a technique which, when performed correctly, can be a safe alternative to correcting sagittal balance of the lumbar spine. Our technique provides a method of producing a large degree of lordosis (up to 45 degrees) with a single level osteotomy, as in a PSO, but without the complications, predominantly blood loss and operative time, as a PSO or SPO.

CONCLUSION

Sagittal plane imbalance is very disabling for patients. It results in intolerable back pain, limitation in mobility, and a poor quality of life. The long-term benefits of restoration of sagittal balance have been previously reported. We present a safe alternative technique for restoring sagittal balance by combining a Smith-Petersen Osteotomy with a large and extreme anterior cage placement.

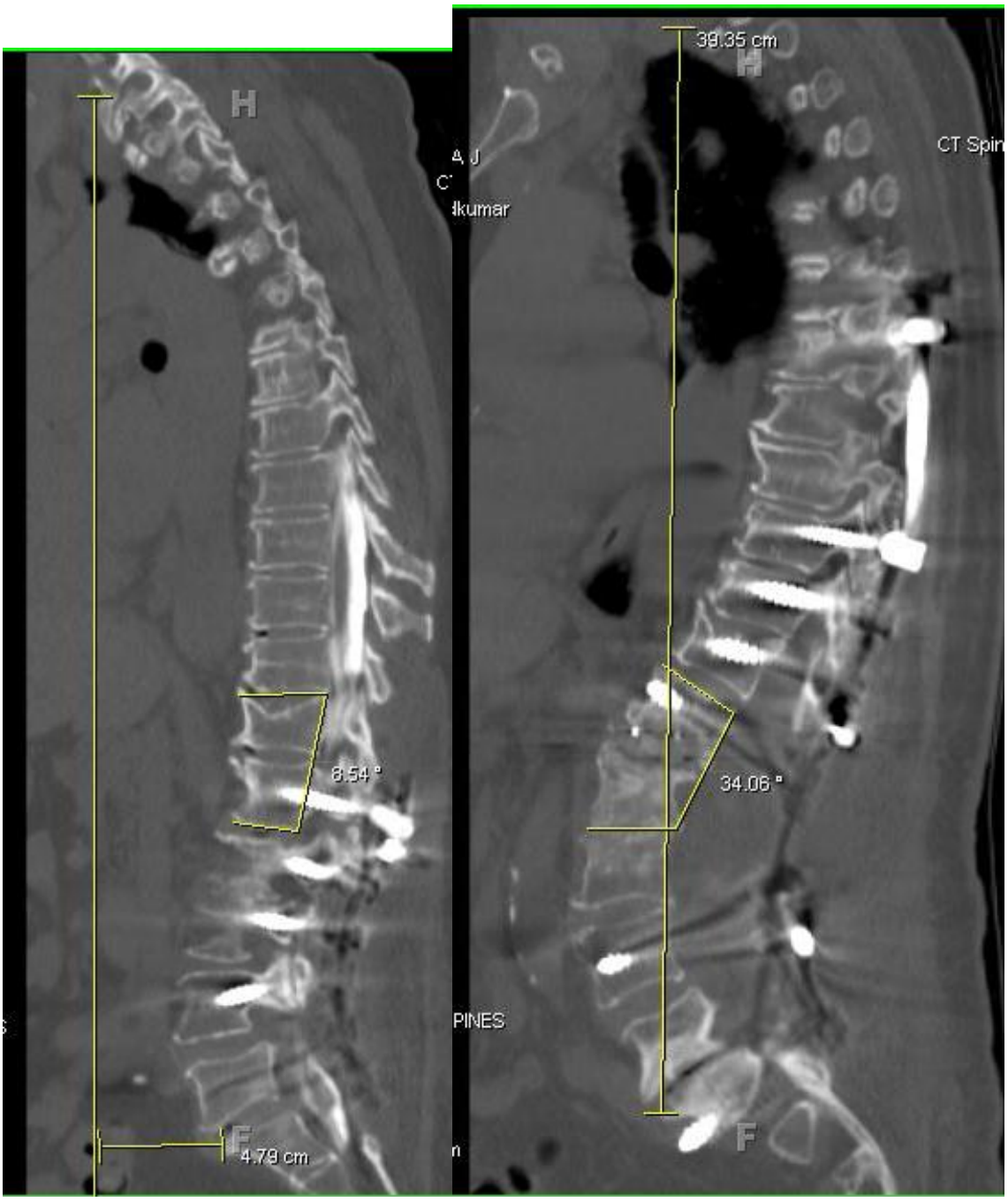

FIGURE 1

Pre-operative (left) and post-operative (right) CT scans of a 78 year old patient who had previously undergone an L1-S1 lumbar fusion. A PSO with extreme anterior cage placement was performed at L1-2 which resulted in a correction of her lumbar lordosis by 42 degrees as well as a 4.79cm correction of her C7 plum line.

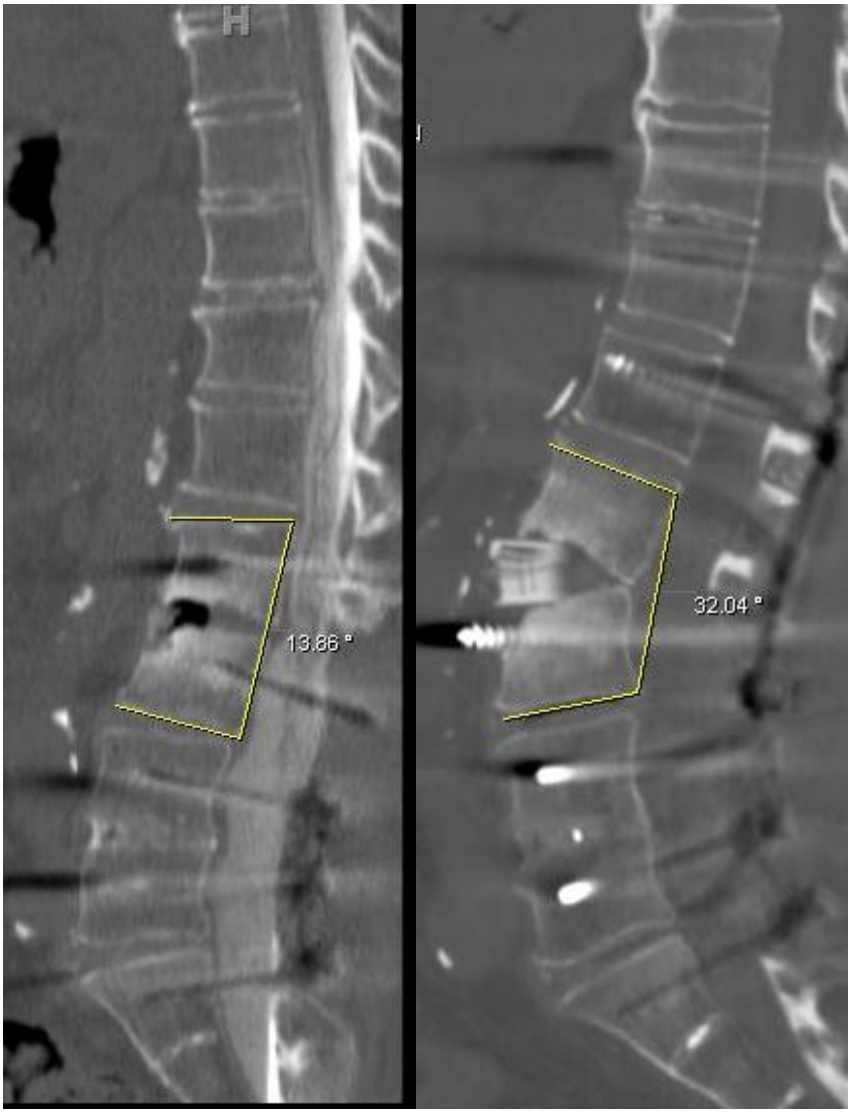

Figure 2:
Pre-operative (right) and post-operative (left) images of at 69 year old male who had previously undergone a L3-S1 fusion. A PSO with extreme anterior cage placement was performed at L2-3 resulting in a 45 degree correction at that level. A postero-lateral fusion was carried up to T11.

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Negative-pressure therapy for deep wound infections following instrumented spinal fusion: retrospective review of twenty-one cases and review of the literature

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Abstract

Introduction: Wound infection following spinal surgery with instrumentation is a significant cause of morbidity. Historically, wounds were aggressively irrigated and debrided; the instrumentation was often removed. Patients would typically need multiple surgical debridements to obtain a clean wound for closure. Controversy now exists regarding hardware removal versus other treatments. Wound VAC (vacuum-assisted closure) therapy may offer an improved way of managing these complications.

Objective: To describe the effectiveness of wound VAC therapy in infected instrumented dorsal lumbar fusion. Wound VAC therapy has been used to treat many types of open wounds, but there are sparse reports of VAC therapy in neurosurgical literature.

Methods: Consecutive patients (n=21) with deep wound infections following dorsal lumbar fusion surgery were retrospectively reviewed. Patients underwent irrigation and debridement in the operating room, placement of wound VAC, appropriate antibiotic therapy, and delayed primary closure of the wound.

Results: Eight men and thirteen women with an average age of 64 years (range 37-81 years) underwent irrigation and debridement of their infected wound with placement of a wound VAC device. An average of 1.6 (range 1-4) procedures were performed following initial VAC placement, including additional irrigation and debridements as necessary, and removal of the wound VAC with primary wound closure. Therapy was continued an average of 20 days (range 2-63 days). All patients tolerated the therapy well and achieved wound closure with maintenance of the spinal instrumentation at 11 to 30 month follow-up.

Conclusions: Based on our series, wound VAC therapy is an effective modality in the treatment of instrumented dorsal lumbar wound infections. All patients achieved a clean wound with retention of their hardware. The literature review revealed 139 of 146 patients (95.2%) achieved a clean wound at follow-up. Mortality was reported for one patient subsequent to blood loss after refusing a transfusion.

Key Words: vacuum-assisted closure, negative-pressure wound therapy, spine, infection, complication

Introduction

Negative-pressure wound therapy, also known as vacuum-assisted closure (VAC), is a technique that promotes wound healing by preparing the wound bed for closure, reducing edema, promoting granulation tissue formation and perfusion, and removing exudates and infectious material.[8] VAC therapy has been reported as successful in the treatment of abdominal, sternal,

and extremity wounds.[7,10,13] This therapy has been utilized at our institution for treatment of deep wound infections in patients with instrumented lumbar fusions.

Wound infections following spinal fusion surgery are challenging for both the surgeon and the patient. Rates of infection have been reported from 0.4-20%.[11] These complications are often treated with repeated irrigation and debridement operations, intravenous antibiotics, and eventual primary closure. Historically, the removal of implanted hardware was strongly advised.[4,15] Other treatments that have been advocated in the literature include: aggressive debridement with primary closure, implanting antibiotic impregnated polymethylmethacrylate beads with or without primary closure, irrigation-suction systems, delayed primary closure, or a combination of the above.[11] Aside from the physical and mental morbidity of this disease process to the patient, the additional cost to the healthcare system can be substantial.[3]

The use of negative-pressure dressing systems has been reported in cardiothoracic, orthopedic, general surgery, and plastic surgery literature. There has been one report of this treatment modality in neurosurgical literature.[9] This retrospective study will outline the utilization of VAC therapy for deep wound infections following instrumented lumbar fusion surgeries at our institution and summarize VAC therapy in the literature.

Clinical Materials and Methods:

Between November 2002 and May 2008, 21 patients with subfascial wound infections following instrumented lumbar spinal fusions had negative-pressure dressing systems placed. All patients presented subsequent to discharge from the neurosurgical service to home, subacute rehabilitation, or inpatient rehabilitation. The charts were retrospectively reviewed with attention to the original surgery date, levels fused, date of VAC placement, dates of additional washout procedures, date of VAC discontinuation, bacteria cultured, and patient comorbidities.

Inclusion and Exclusion Criteria

The inclusion criteria were patients with subfascial wound infections following posterior thoracolumbar or lumbar fusion procedures that were treated with negative-pressure dressing as the initial modality. Exclusion criteria were patients less than 18 years old, deep wound infections of the cervical or thoracic spine, superficial wound infections (above the fascia), and patients with spinal infections prior or subsequent to the fusion treated with a therapy other than VAC.

Protocol

The negative-pressure dressing protocol included empiric antibiotic therapy in the form of intravenous cefazolin (vancomycin in patients with a cefazolin allergy), which was modified as necessary after cultures and sensitivities were obtained. The patients underwent superficial and deep wound cultures, irrigation and debridement, and VAC placement in the operating room.

The infectious disease service was consulted for management of the antibiotic therapy. Wound care nurses performed VAC changes every other day at the patients' bedside. A representative from the neurosurgical service examined the wound during dressing changes. Complications with VAC equipment were addressed by wound care or neurosurgical staff within 60 minutes assuring nearly uninterrupted therapy. The patients underwent additional irrigation and debridement procedures at the discretion of the attending neurosurgeon. When the wound was adequately granulated, the patients returned to the operating room for VAC removal and primary closure.

Results

There were 21 patients, 8 male and 13 female, included in this review. The mean age was 63.5 years, with a range of 37 to 81 years. The patients presented an average of 47.2 days (range 8 – 244 days) after their initial fusion. An average of 2.6 vertebral levels were originally fused, with a range of 1 to 6 levels. Patients had their wounds primarily closed after placement of the VAC dressing without additional irrigation and debridement operations in 13 of 21 cases. One additional washout procedure was performed on 4 patients. Two additional washout procedures were performed on 3 patients. Three additional irrigation and debridement procedures were performed on 1 patient. Patients underwent an average of 1.6 procedures including removal of the VAC device and primary closure after the initial placement of the wound VAC. Mean duration of VAC therapy was 19.6 days, with a range of 2 days to 63 days. All patients achieved a clean, primarily-closed wound without removal of the instrumentation following negative-pressure therapy at a minimum of 11 months follow-up (range 11-30 months).

Wound infection cultures demonstrated multiple organisms in 9 (43%) patients. The most common organism cultured was *Staphylcoccus aureus* in 11 of 21 (52%) patients. Resistance to methicillin was demonstrated in 5 of the 11 *Staphylcoccus aureus* strains. Other common organisms identified were *Entercoccus faecium* (6 of 21 (29%)), *Escherichia coli* (5 of 21 (24%)), *Pseudomonas aeruginosa* (4 of 21 (19%)), and *Staphylcoccus epidermidis* (3 of 21 (14%)). The following organisms were cultured one time each among this series of patients: *Proteus mirabilis*, *Acinetobacter baumannii*, *Morganella morganii*, *Klebsiella pneumonae*, *Corynebacterium minutssimum*, and *Streptococcus pneumoniae*.

All patients in this review suffered from coexisting medical conditions prior to their fusion procedure. The most common condition was hypertension in 16 of 21 (76%) patients. Other comorbidities in descending order were hyperlipidemia, osteoarthritis, asthma, obesity, diabetes, coronary artery disease, hypothyroidism, gastric reflux, depression, anxiety, and a history of cancer.

Discussion

Negative pressure wound therapy has been subjected to many experimental studies. Hunter et al. reviewed this data and concluded that VAC therapy is believed to work by promoting a moist wound environment, creating mechanical forces that stimulate a biological

response, promoting perfusion, reducing edema, altering wound fluid composition, and assisting in granulation tissue formation.[8]

The first wound VAC device was approved by the FDA in May 1995. Use of the device was described in the plastic surgery literature in 1997.[2] Indications included acute wounds, burns, and skin grafts. VAC therapy was subsequently reported in use for wounds of the sternum following cardio-thoracic surgery;[17] pressure ulcers, including diabetic ulcers;[1,16] orthopedic trauma;[6] and open abdominal wounds.[5]

With respect to deep wound infections following spine surgery, there have been several case reports and retrospective reviews in plastic surgery and orthopedic literature.[11,12,14,18-21] One case series was reported in neurosurgical literature.[9] Yuan-Innes et al. first reported the use of vacuum-assisted wound closure for spinal wounds with exposed hardware.[20] The two cases were pediatric patients with wound infections that failed conservative treatment consisting of multiple irrigation and debridements with antibiotic-impregnated bead placement and intravenous antibiotics. One patient received a split thickness skin graft after 6 weeks of VAC therapy. The other patient underwent no further surgeries after 10 weeks of VAC therapy. Both wounds were stable at 6 months and 10 months respectively.

The first case series of vacuum-assisted wound closure management of postoperative deep wound infections after spinal fusions was reported by Mehbod et al. in 2005.[12] In this series, 20 patients underwent an average of 2.2 procedures, including the primary wound closure. All patients tolerated the wound VAC, continued 6 weeks of intravenous antibiotics, and achieved a clean wound without removal of the instrumentation at an average of 10 month follow-up.

In 2008, Ploumis et al. reported a continuation of the study initiated by Mehbod et al.[14] The series discusses the management of 73 consecutive patients with posterior spinal wound infections managed with vacuum-assisted wound closure. Patients required an average of 1.4 procedures, including the primary wound closure. There were 2 cases of uncontrolled sepsis following VAC placement. The remainder of the patients achieved a closed wound without removal of instrumentation at an average of 1 year follow-up.

A retrospective study of 15 patients was reported by Labler et al. in 2006.[11] All patients developed subfascial infections after dorsal spinal surgery and were treated with irrigation and debridement, intravenous antibiotics, and vacuum-assisted closure. Instrumentation was originally placed in 13 patients; it was exchanged in 7 cases, removed in 5 cases, and unaltered in 1 case. Decision to leave, exchange, or remove the implanted material was made based on literature cited in the publication and the authors' clinical experience. Follow-up was possible in 14 of the patients at an average 28.9 months. All wounds healed well with the exception of one new infection which occurred 169 days after the original infection. It was treated again with irrigation and debridement, and negative-pressure therapy; it healed without further events.

Van Rhee et al. presented a series of 6 pediatric patients who underwent spinal fusion to treat scoliosis.[18] The patients averaged 12.6 years (range 6-16 years). All infections occurred within six weeks postoperatively; all cultures grew *Staphylococcus aureus* (one was methcillin-resistant). Wounds were allowed to heal by secondary intention, which averaged 3 months to

complete. All patients achieved wound closure without removing the instrumentation and remained infection-free at an average of 25 months (range 9-42 months) follow-up.

Vicario et al. reported their experience with wound VAC therapy in deep wound infections following spinal fusion for traumatic injury in 2 patients.[19] The patients underwent fusions from T1 to L1 and T8 to L2. They presented 3 weeks and 5 weeks after surgery respectively. Both patients underwent irrigation and debridement with instrumentation exposure, VAC therapy, and intravenous antibiotic therapy. Cultures grew *Staphylococcus aureus* in both patients, and additionally, *Escherichia coli* in one patient. Both patients had granulation tissue with complete coverage of their instrumentation at 2 weeks and 3 weeks respectively. Wound closure was possible at 3 weeks and 4 weeks respectively. Wounds remained well-healed at 6 month follow-up.

A study group of 5 men and 6 women with an average age of 58.7 years (range 40-75 years) who underwent VAC therapy following spinal fusions were reported by Zehnder et al.[21] Subfascial infections were present in 9 patients, 1 patient had infection of the iliac crest donor site, 1 patient had wound dehiscence superficial to the fascia. The mean number of spinal levels originally fused was 6.3 (range 1-15 levels). Patients were treated with VAC therapy an average of 26 days (range 11-47 days), and then primary closure was performed. No patients required additional irrigation and debridement procedures. Removal of instrumentation was necessary for one patient whose fusion was complete. Healing was demonstrated for all patients at an outpatient visit, except one who was lost to follow-up.

Jones et al. presented a series of 16 patients with deep wound infections focusing on complications related to the VAC therapy they experienced.[9] The mean patient age was 52.3 years (range 14-76 years). The mean number of procedures following initial VAC placement was 1.4, with a mean length of VAC therapy of 34.3 days (range 2-118 days). Bleeding complications from the negative-pressure therapy was experienced in two patients; one of whom refused blood transfusions and subsequently died. Reapplication of the VAC dressing was necessary in two patients with persistent infections. A skin graft was placed in one patient due to nonhealing granulation tissue.

The studies are compared in table 1. Among the review series, the range of the mean number of procedures including primary closure following initial VAC placement is 1.4 to 4.8 procedures. The range of the mean time to wound closure after initial VAC placement is 7 to 90 days. Excluding the patients that were allowed to heal by secondary intention, as well as studies with fewer than 11 patients, the range of time to wound closure is 7 to 24 days. Negative-pressure wound therapy was successful in achieving a clean, closed wound at follow-up in all but 7 patients (95.2%).

Conclusions

The case series presented, along with the review of literature, suggests that negative-pressure wound therapy is an effective modality for treatment of subfascial wound infections following instrumented spinal surgery. Further study is needed to assess its superiority to other

treatment methods in terms of efficacy and monetary savings to the healthcare system. Additionally, wound VAC therapy is not without risk; patients should be advised that bleeding, nonhealing, and reinfeciton are rare, but does occur.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Simultaneous choroid plexus carcinoma and pilocytic astrocytoma in a pediatric patient: case report and clinical considerations

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Summary
Simultaneous primary brain tumors in the pediatric population without prior chemotherapy or radiotherapy, phacomatosis or known familial history are a rare occurrence. The authors report the case of a 4-year-old male with simultaneous choroid plexus carcinoma and pilocytic astrocytoma with features of oligodendroglioma. Magnetic resonance imaging studies revealed diffuse heterogeneously enhancing left intraventricular and posterior fossa tumors initially believed most consistent with multicentric choroid plexus carcinomas. A multiple staged surgical resection was carried out for each tumor with successful gross total resection. Upon gross inspection intra-operatively as well as confirmed by histological analysis postoperatively, two distinct simultaneous tumors were identified: choroid plexus carcinoma and pilocytic astrocytoma. To our knowledge this is the first case report published identifying two distinct tumor types with similar radiographic appearances in a pediatric patient with no prior history of radiotherapy, chemotherapy or phacomatosis.

Introduction

The clinical dilemmas faced by neurosurgeons in the treatment of multiple intracranial tumors were first thoroughly described by McCormick, Batsdorf and Malamud over fifty years ago after a landmark study by Bailey and Cushing contributed significantly to our arsenal of knowledge about the mode of growth and spread of gliomas.[1, 27, 31] At that time, simultaneously occuring primary tumors were usually found in post-mortem examinations and even then considered a rare occurrence. Several smaller reports followed; however, Courville was first to focus attention on multiple primary brain tumors during the modern medicine era which then was only able to account for 25 cases of multicentric or multiple gliomas in his entire review.[7] Much confusion existed surrounding the best classification of multiple tumors until a report by Russell and Rubenstein classified multiple intracranial tumors into two categories that are still currently utilized today: multiple tumors and multicentric tumors.[48] Multiple tumors were interpreted to

result as dissemination by an "established" route such as via the commissural or other pathways, spread via the cerebrospinal fluid or through local metastasis through satellite formation in the immediate vicinity of the initial tumor. Multicentric tumors are widely separated lesions in different locations that do not easily fit into one of the aforementioned pathways of dissemination. More recent published reports document multiple or multicentric intracranial neoplasms usually occurring in patients with antecedent chemotherapy or radiotherapy and/or developing secondary neoplasms, those patients with known genetic histories putting them at increased risk or those with multiple tumors occurring at different times.[4,9,47,51]

Phacomatoses, such as neurofibromatosis and tuberous sclerosis have been shown to be associated with an increased incidence of multiple tumors.[26,47] Recently, genetic analysis has allowed for patients with germ line mutations to be identified. Mutations in several genes including TP53, hSNF5/INI1, as well as other chromosomal abnormalities have led to the identification of several genes involved with multiple tumor syndromes such as Li-Fraumeni, Aicardi X and Turcot Syndromes.[39,49,52]

A MEDLINE/PUBMED review utilizing the search terms ("simultaneous tumors" "multicentric tumors" "multiple tumors" "multiple tumors" "two primary intracranial tumors") by these authors reveals only approximately 50 documented cases of simultaneously occurring primary brain tumors.[58] In this group analyzed, only a ten cases have been documented to occur in the pediatric population. The incidence of multiple and multicentric tumors reported in the literature varies greatly. Much of the data on incidence of these tumors is taken from poorly controlled studies in the pre-imaging era excluding all but gliomas. From these studies, multiple intracranial glial neoplasms have been inferred to occur with from 2-10%; with the incidence of two simultaneously occurring tumors of different histology occurring simultaneously is estimated to be far less. From 1896 to 1959, an analysis of twelve series of over 1200 patients reported an incidence ranging from 1-10%.[27] Albeit, choroid plexus carcinomas are decidedly of neuroectodermal origin, and are even more rare, representing less than 0.5% of all central nervous system tumors with an annual incidence of 0.3 cases per 1 million population.[16,32,62] The following case illustrates the first published report of two simultaneously occurring brain tumors with similar radiographic appearances in a pediatric patient without prior history of radiation, chemotherapy or known phacomatoses.

Case Report

History and Examination: A 4 year-old Caucasian male was transferred to our institution from an outside hospital with a five-day history of headache, anorexia, nausea and emesis. He had been doing well until one week prior to admission when he began to develop symptoms of an upper respiratory infection in the form of nasal congestion and low-grade fevers for which his mother had been giving him an over-the-counter nasal decongestant with minimal relief. His symptoms

worsened and he developed intractable non-projectile vomiting associated with headache. The headache was frontally located, sharp in quality and caused fussiness and irritability eventually causing him to cry inconsolably. His mother noted that after emesis there were periods of relief, however, the frequency of these episodes were increasing up to 4-5 times daily. He was observed to be sleepier and less active, with a clumsy gait and exhibited periodic bizarre truncal body movements. Weakness, numbness, paresthesias, night sweats, weight loss, rashes, back pain and recent trauma were denied.

The patient is a product of a normal spontaneous pregnancy from two nonconsanguineous parents without complication, significant medical or surgical history. Developmentally, he is physically appropriate for age except for a speech delay with a 75% understandable speech rate, for which he is currently under evaluation. Immunizations are current. There is a sporadic family history of stomach and esophageal cancer, lymphoma in a paternal great-grandfather who died at fifty years of age, seizure disorder and kidney disease. There were no first or second-degree relatives with malignancy identified.

Neurological examination revealed a sleepy but arousable child. He was following commands and verbalizing few strings of words with slow pentameter and devoid of complex sentence usage. Fundoscopic examination revealed bilateral papilledema. There were no focal motor or sensory neurological deficits at the time of initial examination.

Radiographic Studies: Review of a non-contrast axial computerized tomography scan of the head performed at an outside institution revealed two separate hypodense cystic masses; one located in the left thalamus and lateral ventricle and a second in the posterior fossa adjacent to the fourth ventricle. There was mass effect and midline shift with associated obstructive hydrocephalus (**Figure 1A, 1B, and 1C**). Initial magnetic resonance imaging of the brain (with and without gadolinium contrast) revealed a 5x2x3 centimeter heterogeneously enhancing, left lateral ventricular lobulated mass with non-enhancing cystic components located laterally and posteriorly. There was associated edema and mass effect upon the thalamus and third ventricle. Within the posterior fossa, a 4x4x3 centimeter heterogeneously enhancing midline mass with extension through the fourth ventricle was found. Again, an associated non-enhancing cystic component located within the fourth ventricle was seen (**Figure 2A, 2B and 2C**).

Management: Immediate staged resection of the supratentorial tumor proceeded by the infratentorial tumor was undertaken in view of the patient's condition, neurological status, hydrocephalus and associated midline shift. Debulking, resection of the intraventricular tumor and placement of an external ventricular drain was performed with the assistance of Stealth (Medtronic, Inc.) intraoperative guidance. A high left parietal circular craniotomy and corticectomy was performed. The tumor was found to be vascular requiring circumferential tumor resection from normal brain prior to intratumoral decompression with use of CUSA

(Inegra Lifesciences Corp.). Successful tumor resection and coagulation of the remaining ventricular choroid plexus was achieved. Post-operative magnetic resonance imaging of the brain (with and without gadolinium contrast) revealed successful resection of the intraventricular tumor (**Figure 3A, 3B and 3C**). Next, our attention shifted to the posterior fossa tumor. On the following day, a suboccipital craniotomy and microsurgical resection was performed. Grossly, the tumor appeared grayish, firm, not clearly defined and not as highly vascularized as was seen during the supratentorial tumor resection above leading one to speculate that these may represent tumors of differing pathology. The patient required re-operation for residual tumor two days after the second staged resection. Post-operative magnetic resonance imaging of the brain (with and without gadolinium contrast) revealed successful resection of the posterior fossa tumor (**Figure 4A and 4B**). Neuro-electrophysiological monitoring was utilized during all resections with no changes from baseline. Tissue samples were sent for pathological analysis. Surveillance magnetic resonance imaging of the axial spine (with and without gadolinium contrast) did not reveal any evidence of drop metastasis. He had a stable post-operative course and was discharged home 5 days later with minimal ataxia.

Chemotherapy was administered according to the CPT SIOP 2000 protocol (choroid plexus tumor study of the Société Internationale d'Oncologie Pédiatrique)[15,65] consisting of the drugs etoposide, carboplatin and vincristine. He received a total of six cycles of etoposide, carboplatin and vincristine over a span of eight months and had no hospitalizations for neutropenia or fever. During the fifth cycle of chemotherapy, he developed gross hematuria and proteinuria, and underwent renal biopsy which revealed immune complex mediated crescentic necrotizing glomerulonephritis. He was prescribed a short-course of prednisone with prompt resolution of his renal symptoms. Due to the development of glomerulonephritis, carboplatin was eliminated from his last cycle of chemotherapy.

Follow-up MRI Brain and complete axial spine (with and without contrast) as well as cerebrospinal fluid analysis performed after his last cycle of chemotherapy failed to show any evidence or recurrence of malignancy. No further chemotherapy or radiation therapy is planned. He will be continued on Bactrim prophylaxis against Pneumocystis carinii for six months following his completion of chemotherapy at which time he can then receive any of his outstanding immunizations delayed due to concomitant chemotherapy. Close monitoring of patient's neurological status as well as serial MRI will dictate future treatment.

Approximately nine months have passed since his initial diagnosis and he is doing well without focal neurological deficits. His cognition, aptitude and physical development is appropriate and he is reaching recommended developmental milestones. He continues to perform physical therapy several times weekly. Language analysis reveals similar delays seen pre-operatively, however, without overt notice clinically. He is able to speak in sentences and comprehend adequately, however, reportedly delayed for his age. Speech therapy has been initiated.

Histological Diagnoses: Grossly, the intraventricular tumor revealed tan, ragged tissue that microscopically showed papillae lined by crowded moderate sized epithelioid cells as well as sheets of cells with abundant cytoplasm. Tumor cells showed focal atypia. Brain invasion of tumor cells was seen focally at the periphery. Mitotic activity was brisk and a high proliferation index was seen with Ki67 immmunostaining. It was felt that this tumor was compatible with a choroid plexus carcinoma (**Figure 5**). Microscopically, the posterior fossa tumor revealed features consistent with both pilocytic astrocytoma and oligodendroglioma. The pilocytic component consisted of mildly pleomorphic astrocytes with oval and minimally tapered nuclei. Rosenthal fibers and densely fibrillar piloid material was also present. A prominent nesting pattern was seen in the tumor confined to the subarachnoid space. The oligodendroglial component consisted of cells with more round nuclei, perinuclear cytoplasmic clearing, abundant capillary network and calcifications. Tumor cells showed immunoreactivity with glial fibrillary acidic protein (GFAP) and immmunostaining with Ki-67 showed a low proliferative index. It was felt that this tumor was compatible with a pilocytic astrocytoma with oligodendroglial features (**Figure 6**).

Discussion

Few reports of simultaneously occurring primary brain tumors without concomitant radiotherapy, chemotherapy or history of phacomatosis have been reported in the literature. To our knowledge, this is the first documented case that has been reported in a pediatric patient. In patients who present with multiple intracranial neoplasms, diagnoses can be demanding, especially when compounded in the pediatric patient population. One must consider that there is not always a clear history and when one is available, it is usually relayed second hand from involved friends or family members. Additionally, there may be absent or conflicting localizing signs present. In our patient, the language delay was suggestive of a lesion localized to the left hemisphere, however, the ataxic gait suggested a lesion localized to the posterior fossa creating clinical confusion and difficulty in precise localization. In the pre-imaging era or in areas without computed tomography or magnetic resonance imaging available, diagnoses may be dangerously delayed. Once radiographic studies are undertaken, both neurosurgeon and radiologist must critically analyze their interpretation. Often alluded to as the "open box" theory, multiple mass lesions with neoplastic, traumatic or cerebrovascular etiologies, when separated by space will act independently and, in some cases, balance the mass effects of one another.[56] It is when the cranial vault is opened or tumor decompressed that further brain shift may occur. Paradoxically, for global malignant cerebral edema the additional space created by allowing brain to herniate through a bone defect site allows tissues to expand so that CT-demonstrated changes initially observed when surgery is not performed are minimized or completely resolved in the postoperative period.[21,44,45] For example, two masses located in contralateral frontal cerebral hemispheres may cancel the mass effect of each independently causing what appears to be

minimal effect to the midline. However, in cases involving multiple brain tumors, the mass effect created by a single tumor is only appreciated only after the other tumor is resected. This has important surgical implications that must not be understated.

Surgical planning with multiple tumors adds more variables to be considered. When planning surgical approaches to multiple tumors we must be cognizant of the shifts that may occur during surgery. In multiple tumors located in anatomic proximity, this may be less of a concern. However, if a single staged approach is used to resect tumor located distantly, deleterious shifts can occur. Several reports have highlighted this phenomenon with resultant fatal ascending transtentorial herniation.[42,58] Nonetheless, many advocate removal of both tumors in one session yielding the best outcomes.[43] If the histological diagnoses is known preoperatively, then those types of tumors with increased likelihood for post-operative edema should be removed last after tumors that are more benign are removed first. Glial tumor resection with resultant post-operative edema may lead to grave results if operated prior to surgery for tumors with more benign pathology due to decreased brain compliance from the coexistent lesion.[29,54] Several others decide on which tumor to remove based upon clinical findings alone.[8,22] Tumors causing most clinical signs are removed first. This is especially important when dealing with superficial and deep simultaneous tumors which may not necessarily require resection if resection of the symptomatic more superficial lesion is successful. Considering these shifts, if computer-assisted neuronavigation is utilized it must be appropriately adjusted to take into account some of the shifts which may have occurred. In our patient, we chose to perform a staged resection. This sequential staged resection was chosen for several reasons including the reasons discussed previously, surgeon preference as well as our ability to repeat imaging studies after each resection for more accurate localization increasing our precision from any shifts that may have occurred.

Choroid plexus tumor management would be greatly facilitated by an accurate, noninvasive, preoperative diagnosis. Current imaging modalities have been inadequate in differentiating these tumors.[23,60] Although choroid plexus tumor was considered, no confirmatory tissue diagnosis had been made preoperatively. Confirmation of pathology aids in preoperative planning, as these tumors are usually hypervascular. Preoperative embolization of hypervascular tumors has been described for decades as an adjunctive technique purported to decrease operative blood loss, operating times and favor larger and more complete resections.[5,17] Supraselective embolization of tumoral feeding arteries have now become standard at some institutions. However, in the pediatric population, preoperative embolization of these feeders has rarely been reported due to their small size and tortuosity in the pediatric population.[36] Given his declining neurological status, a delay in treatment may have been deleterious. Further, it is difficult to ascertain if the true risk associated with this procedure would have been outweighed by its benefit as risk analysis has yet to be determined. Overall, mortality rates from complications related to surgery have ranged from 0-25% and mortality rates attributed to blood loss are reported to be as

high as 12%.[10,33,38] Attempts to use preoperative embolization in pediatric patients have yielded mixed results with many institutions choosing to forego endovascular treatments in this population. As more advancement in microcatheter and microguidewire technology evolve, these patients may have more successful outcomes with these techniques.[36] Additionally, endovascular techniques may also be utilized as a salvage measure for operative or peri-operative control of head and neck vascular injuries in the proper setting.[17] Sensitive, noninvasive diagnostic tools may have assisted us with peri-operative surgical planning; specifically, surgical approaches and adjuvant therapy, such as preoperative embolization, properly planned to address the observed hypervascularity of choroid plexus tumors.

Multiple familial syndromes and phacomatoses have been described which may predispose patients to having multiple tumors on presentation. Neurofibromatosis and tuberous sclerosis are two of the most common syndromes found to have an increased incidence of multiple tumor growth and have been described extensively in the literature.[26,43] Briefly, multiple café au lait spots, axillary and inguinal freckling, multiple discrete dermal neurofibromas, and pigmented iris hamartomas (Lisch nodules) characterize Neurofibromatosis 1 (NF1). Learning disabilities are present in approximately 50% of individuals with NF1. Scoliosis, vertebral dysplasia, pseudarthrosis, and overgrowth are the most serious bony complications of NF1. Less common but potentially more serious manifestations include plexiform neurofibromas, optic and other central nervous system gliomas, malignant peripheral nerve sheath tumors, osseous lesions, and vasculopathy. Neurofibromatosis 2 (NF2) is characterized by bilateral vestibular schwannomas with associated symptoms of tinnitus, hearing loss, and balance dysfunction. Age of onset is usually 18 to 24 years with nearly all affected individuals developing bilateral vestibular schwannomas by the age of 30 years. Affected individuals may also develop schwannomas of other cranial and peripheral nerves, meningiomas, and rarely, ependymomas and astrocytomas. Diagnosis of NF is based on clinical criteria. NF2f is the only gene known to be associated with neurofibromatosis type 2 and is currently being used as a confirmatory test once clinical diagnosis is made. Tuberous sclerosis is an autosomal dominant genetic disorder affecting cellular differentiation and proliferation, which results in the formation of hamartomas in several organs including skin, brain, eye, kidney, and heart. The frequency in the United States is 1 case in 5,800-30,000 persons. It is usually diagnosed in childhood, with cardiac and cortical tuber development, while skin lesions are seen in more than 90% of patients at all ages. Multiple major and minor features are considered and used in the diagnoses described elsewhere.[14,40,46] Of interest to our patient, a major diagnostic criteria is the development of astrocytomas. Other less common syndromes include Basal cell nevus syndrome (Gorlin-Gortz syndrome) and Turcot's syndrome.[2,18] It is critical that these most common syndromes be considered when in evaluation of the entire patient who presents with multiple neurological pathology.

The occurrence of two simultaneously occuring tumors of infancy in the same family is a rare event and suggests the presence of a germline mutation with a predisposition to malignancy.[55] Choroid plexus carcinomas and other multiple primary brain tumors have been associated with several familial neoplastic syndromes including Li-Fraumeni, Aicardi and Turcot. Data is sparse regarding the precise mechanisms involved due to their infrequent nature as well as multifactorial etiologies. A variety of somatic and germ cell line mutations have been implicated including the TP53 and hSNF5/INI1 genes as well as X-linked chromosomal abnormalities. The TP53 gene is located on 17p13.1 and expresses the protein product p53, which influences tumor suppression via a variety of mechanisms including DNA repair, apoptosis, cellular differentiation, and angiogenesis.[53] TP53 gene mutations with loss of p53 function as well as prolongation of the half-life of the protein producing the oncological effects seen. Choroid plexus carcinomas are one of the tumors found in Li-Fraumeni families with TP53 germline mutations.[20,28] The hSNF5/INI1 gene is located on 22q11.2 encoding a unit of SWI/SNF adenosine triphosphate dependent chromatin-remodeling complex.[52] Genetic studies of families with this mutation, have identified the development of both renal and extrarenal malignant rhabdoid tumors, choroid plexus carcinomas, atypical teratoid rhabdoid tumors, and medulloblastomas.[55]

In our patient, no stigmata of phacomatoses were identified. His external examination did not reveal any skin lesion nor was there any history of masses or other lesions. Fundoscopic examination revealed papilledema but no evidence of Lisch nodules or other intraocular pathology. There was a family history of sporadic age-related neoplasm, but no familial tumors identified. Radiographic studies did not reveal any masses in the cerebellopontine angles nor evidence of intraparenchymal tubers suggestive of neurofibromatosis or tuberous sclerosis, respectively. Echocardiogram did not reveal any cardiac abnormality or lesions. DNA analysis was negative for TP53 gene mutations and there was an absence of a defect in the NF2 gene. hSNF5/INI1 gene was positive, indicating normal genotype pattern. hSNF5/INI-1 gene is involved with several atypical teratoid and rhabdoid tumors and helps to distinguish these tumors (which are negative for immunochemistry stain with INI-1 antigen) from choroid plexus carcinoma which will stain positive. In this case, a positive staining for INI-1 helps to confirm the pathological diagnosis of choroid plexus carcinoma. Chromosomal analysis failed to show any mutations. Microarray analysis of oligodendroglial tumor component failed to show 1p or 19q deletions / duplications. Although studies showing the association between p53 mutations and choroid plexus carcinoma have predominantly been seen in adults, it is not entirely clear if children with this same mutation will phenotypically express the neoplasms as well. Unlike in their adult counterparts, pediatric astrocytomas are characterized by a low incidence of p53 mutations.[3] Genetic studies in patients with secondary neoplasms due to familial neoplastic syndromes have concluded that the incidence of p53 mutations among pediatric patients with astrocytic tumors is low and, unlike in adult patients, p53 mutations do not play an important role in their development.[24] Further genetic testing performed on all pediatric brain tumors will allow

more detailed understanding of the pathogenesis of these uncommon and often deleterious cancers.

The optimal treatment for pediatric choroid plexus tumors is currently unknown and the precise role adjunctive chemotherapy and/or radiotherapy has in its treatment currently being investigated.[15,37,38,65] The ongoing SIOP 2000 protocol for patients with choroid plexus tumors is a prospective registry and randomized study for children and adults with choroid plexus tumors. Treatment consists of maximal surgical resection, and for those with choroid plexus carcinoma, postoperative chemotherapy and delayed radiation for patients >3 years old. Goals of the study are to compare response rates, survival, and tumor resectability after chemotherapy randomized to carboplatin or cyclophosphamide backbones. This protocol is currently being utilized at a number of international cancer centers in both Europe and the United States and results are forthcoming.

Even though there is no defined treatment for multiple tumors, we chose to tailor treatment towards the pathology with most aggressive natural history: choroid plexus carcinoma. Our patient was treated with a well-established chemotherapy protocol that is being utilized internationally. Based upon his gross total resection at the time of initial diagnosis, and in his duration of eight months of chemotherapy, no further evidence of recurrence both clinically and radiographically by MRI, it was elected to withhold planned radiation treatments. It is well documented that radiotherapy may cause significant neurocognitive delays and its use is currently being questioned.[13,63,64] Further, in the setting of his renal condition coupled with potential adverse effects, significant issues regarding his quality of life were viewed as greater risk than benefit. An important result of the SIOP 2000 study thus far is that international collaboration on treatment for these rare tumors is possible; this may serve as a future model for collaboration in other rare pathology. Ultimately, the optimal treatment will depend on multiple factors including pathology, extent of resection, comorbidities, and quality of life and must be tailored for each patient on an individual basis.

Reports of multicentric or multiple tumors are not uncommon and have been previously reported in the literature.[8,22,41,57] Multiple hypotheses have been proposed but all remain unproven. Currently, no plausible pathophysiology exists to explain simultaneously occuring primary brain tumors of varying histology. In a retrospective case review compiling patients from over two decades, 57 patients with diagnoses of meningiomas and glial tumors were examined. Giunta found many of the cases to have conflicting results, including improper or missing diagnoses and varying treatments as evidenced in the pre-CT, pre-MRI and pre-microsurgical era of neurosurgery.[54] Further, many cases included patients with recent treatments of radiation therapy or chemotherapy which has already been described. Only four of twenty-four patients were reported in the CT era as having a preoperative verification of both tumor types. This further confounds the little data that we have available to study as well as adds to the uniqueness of our

case presented here. Studies of the pathogenesis of multiple tumors have looked at cerebrospinal fluid channels for answers. Ependymomas have a known disposition to spread and seed at other distant sites through these channels. Given their predominant location, these tumors are usually located with ample access to cerebrospinal fluid and it is possible that certain tumors will grow in areas with substrates that are advantageous for their growth and proliferation.[66] More recently, others have proposed that local mechanisms may be partly responsible for simultaneous tumor formation proposing that astroglial irritation may cause local cellular transformation leading to adjacent gliotic changes and tumor formation.[57] It is reported that as much as 32% of multiple tumors had their tumoral localization in juxtaposition increasing the possibility that one tumor may act as an irritating agent inducing local proliferation of the other.[6,30,54] This can be partially explored when looking at brain tumors that have been found to be composed of two separate distinct histopathological diagnoses in the same tumor.[11] If a local "crosstalk" does exist between simultaneously occuring tumors, one might expect the incidence to be higher than is currently observed. In our patient, histological examination did not reveal features which would be distinguishing from other independently occuring tumors. The histology identified two tumors that had no variations greater than those observed in different regions of single tumors. It is feasible that further genetic testing or microscopy not yet clinically utilized might be able to discern features of these tumors suggesting a "crosstalk" communication or propensity for multicentricity which is not currently available. Russell and Rubinstein suggested the possibility of coincidental multiple primary brain tumors and Kuroiwa et al. reached the same conclusion after analyzing 116 cases of multiple intracranial tumors not associated with NF1.[19,48] They found that the most frequent combinations were meningiomas and gliomas, meningiomas and pituitary adenomas and meningioma and neuromas. Since these represent relatively common tumors, it is possible that several multiple tumors incidentally coexist. It appears plausible that he may have had a *de novo* mutation of a yet unknown tumor suppressor gene(s) or may just have fallen the victim of coincidence.

Based upon the Conheim Theory of Embryonal Rests, Ostertag in 1942 [34,35] proposed that tumors grew from primitive cells which were displaced during embryogenesis and the development of the central nervous system. These cells when in the presence of multipotent cells had a propensity to multiply with blastomatous potential phenotypically presenting in later life to develop into coordinated "blastomas" throughout the nervous system. His theory was *blasted* down at that time as he could not explain the time delay between the development of the brain and clinical manifestations nor could he find evidence of such multipotent cells with the technology then available to him. However, we now know that stem cells are ubiquitously found throughout the central nervous system likely having an active role in tumor formation and control.[25,61] Stem cells when in the presence of cells with germ line mutations are at increased predisposition for uncontrolled "blastomatous" cellular growth ideal for tumor formation, thereby providing some theoretical support to Ostertag's early theory.

Conclusion

In this report, we describe the first published case of a pediatric patient with both choroid plexus carcinoma and pilocytic astrocytoma with oligodendroglial features. Initial radiographic interpretation led to an impression of multicentric glioma or multicentric choroid plexus carcinoma, however, histopathology revealed two very distinct tumors. This has important implications for clinicians in regards to diagnosis and treatment planning. Our current knowledge of the origin, growth and genetics of multicentric and multiple tumors is not very well understood in the pediatric population and begs for further study in order to optimize patient treatment and outcome.

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Disclosure or Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Figure Legend

Figure 1A-1C: Non-contrast axial computerized tomography scan of the head demonstrates hypodense and cystic lesions of the left lateral ventricle and posterior fossa. Note obstructive hydrocephalus and midline shift present

Figure 2A-2C: Gadolinium-enhanced magnetic resonance imaging of the brain axial (A, B) and sagittal sequences (C) demonstrate left lateral ventricle and posterior fossa enhancement of suspected multicentric choroid plexus carcinoma or glioma

Figure 3A-3C: Gadolinium-enhanced magnetic resonance imaging of the brain after first staged resection of left lateral ventricle lesion. Axial (A), sagittal (B) and coronal (C) sequences demonstrate gross total resection of left lateral ventricular supratentorial enhancing lesion with improvement of midline shift

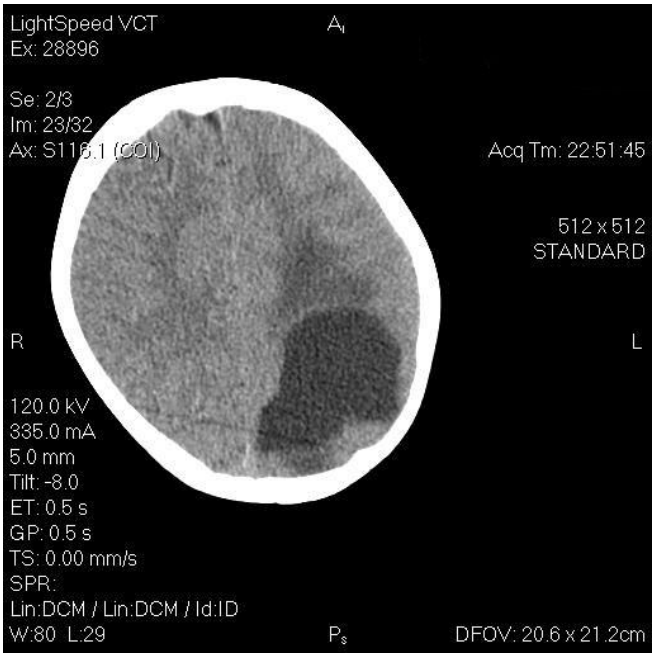
Figure 4A and 4B: Gadolinium-enhanced magnetic resonance imaging of the brain after second staged resection of posterior fossa lesion. Axial (A) and sagittal (B) sequences demonstrate gross total resection of posterior fossa enhancing mass

Figure 5: Sheets of atypical cells in the solid choroid plexus carcinoma. (Hematoxylin & Eosin magnification X 200) *Inset*: Scattered atypical cells lining well-defined papillae of choroid plexus carcinoma. (Hematoxylin & Eosin magnification X 200)

Figure 6: Oligodendroglial pattern with small cells with round uniform nuclei and perinuclear clearing, delicate capillaries and calcifications in low-grade astrocytoma (Hematoxylin & Eosin magnification X 100). *Inset*: Densely fibrillar "piloid" areas of low-grade astrocytoma involving the subarachnoid space. (Hematoxylin & Eosin magnification X 200)

Figure 1A-1C: Non-contrast axial computerized tomography scan of the head demonstrates hypodense and cystic lesions of the left lateral ventricle and posterior fossa. Note obstructive hydrocephalus and midline shift present

Image 1A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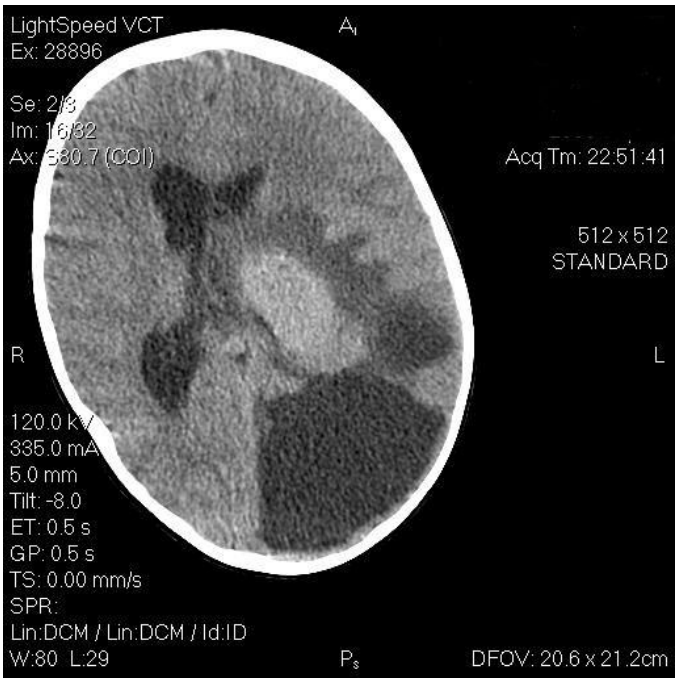
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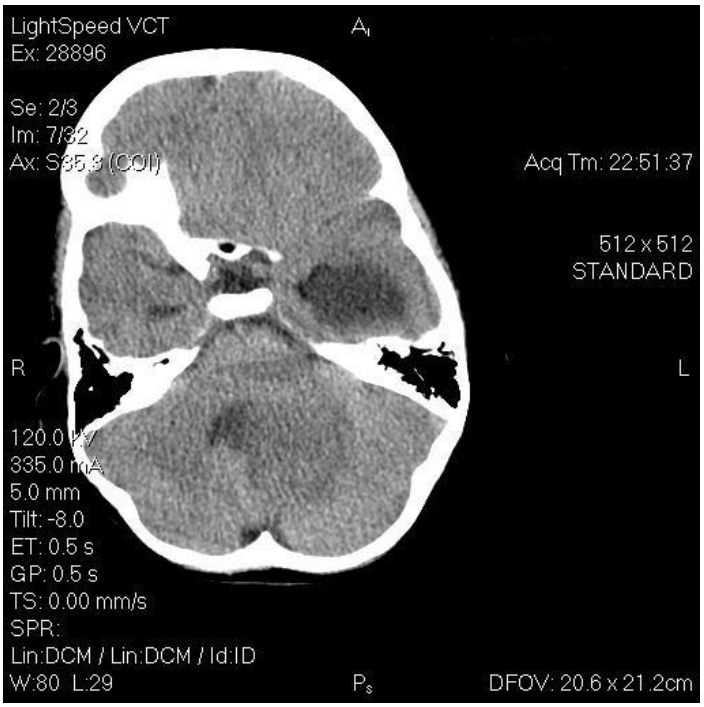
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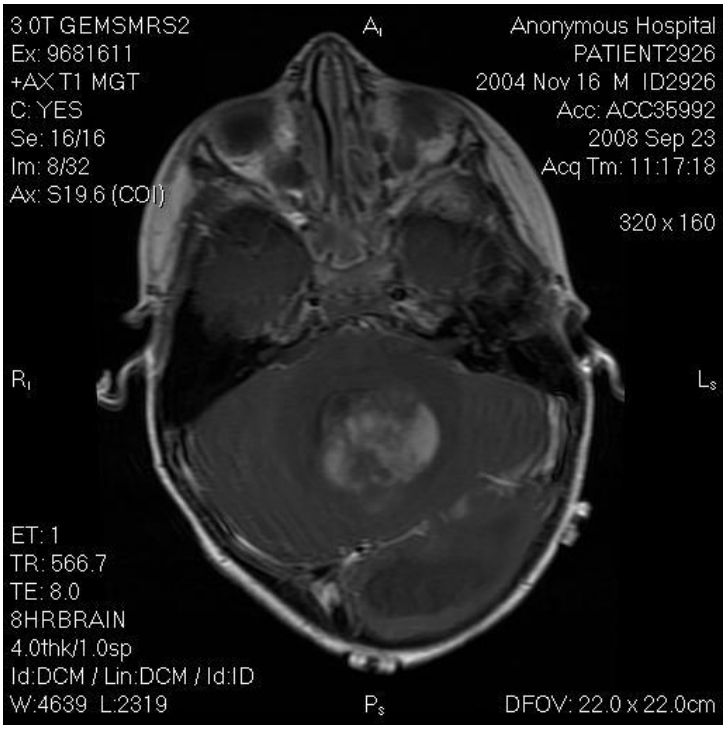
Figure 2A-2C: Gadolinium-enhanced magnetic resonance imaging of the brain axial (A, B) and sagittal sequences (C) demonstrate left lateral ventricle and posterior fossa enhancement of suspected multicentric choroid plexus carcinoma or glioma

Image 2A



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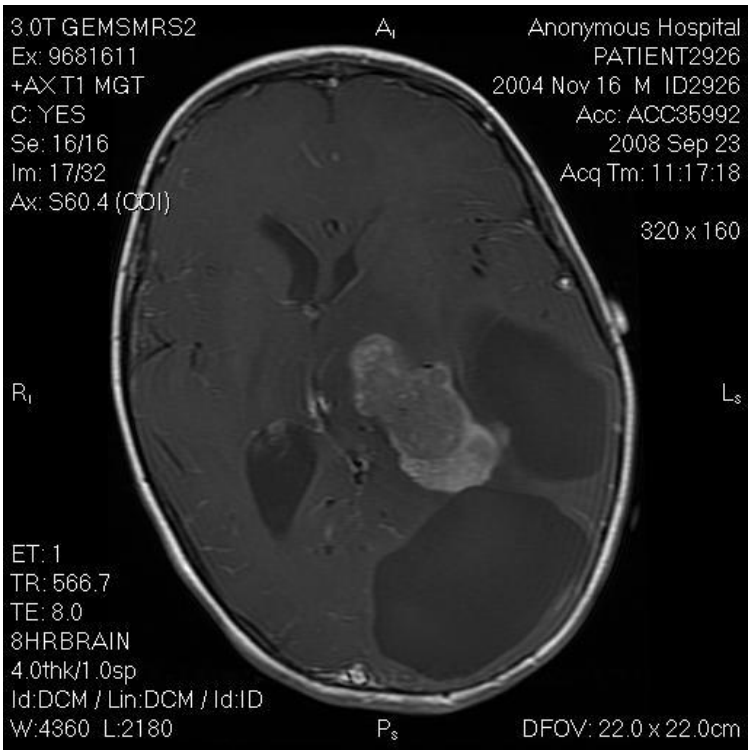

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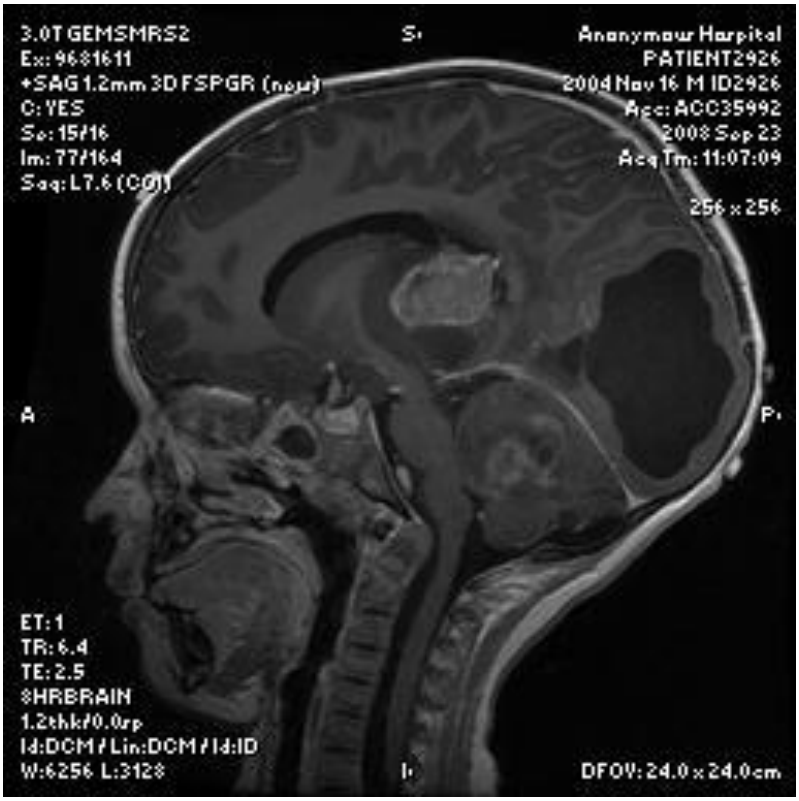
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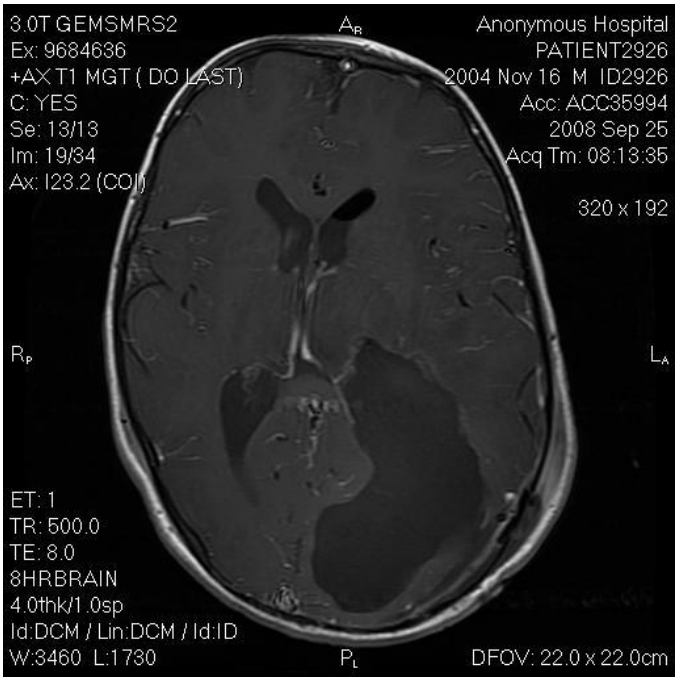
Figure 3A-3C: Gadolinium-enhanced magnetic resonance imaging of the brain after first staged resection of left lateral ventricle lesion. Axial (A), sagittal (B) and coronal (C) sequences demonstrate gross total resection of left lateral ventricular supratentorial enhancing lesion with improvement of midline shift

Image 3A



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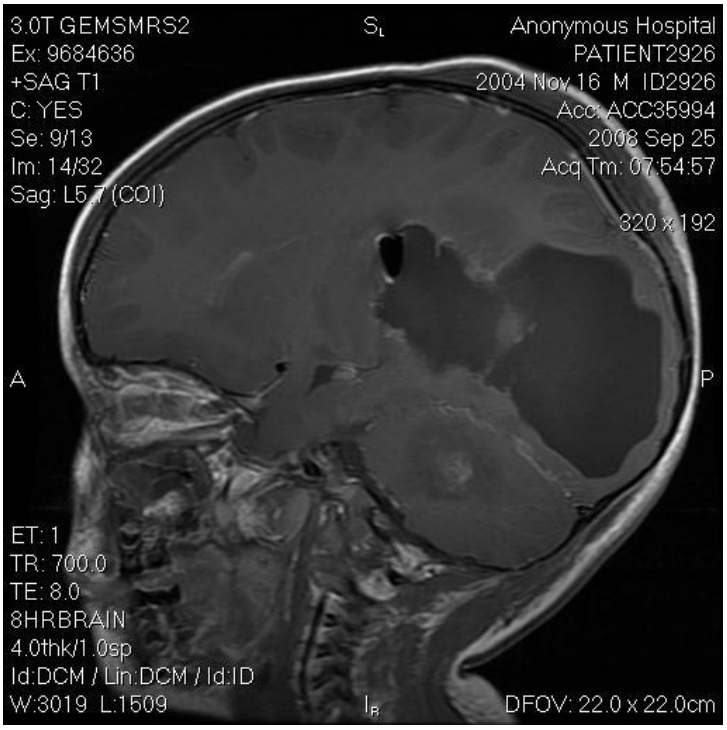
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Image 3C

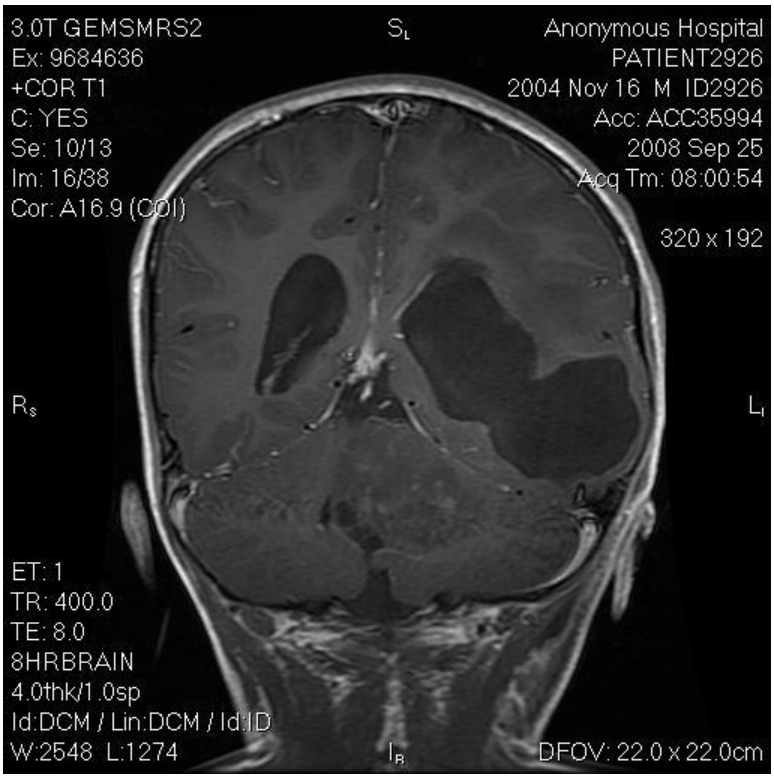
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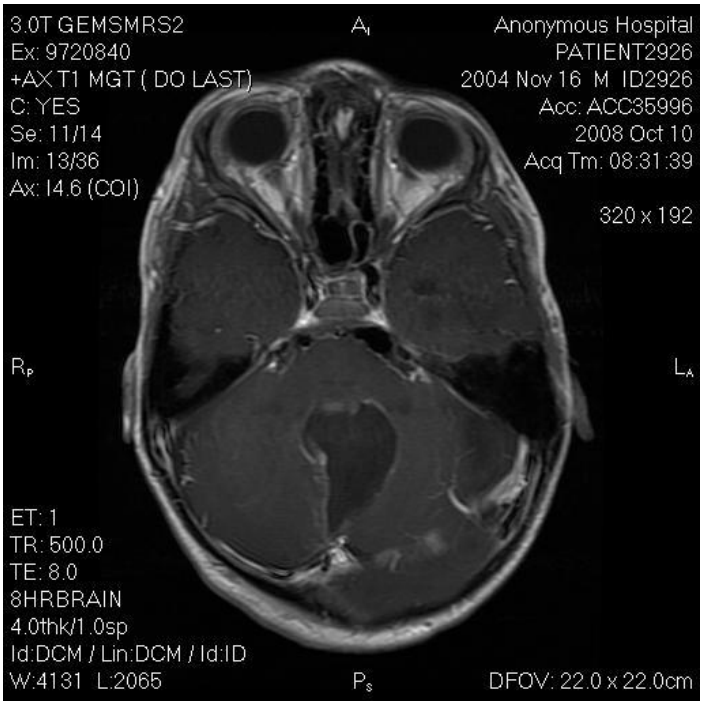
Figure 4A and 4B: Gadolinium-enhanced magnetic resonance imaging of the brain after second staged resection of posterior fossa lesion. Axial (A) and sagittal (B) sequences demonstrate gross total resection of posterior fossa enhancing mass

Image 4A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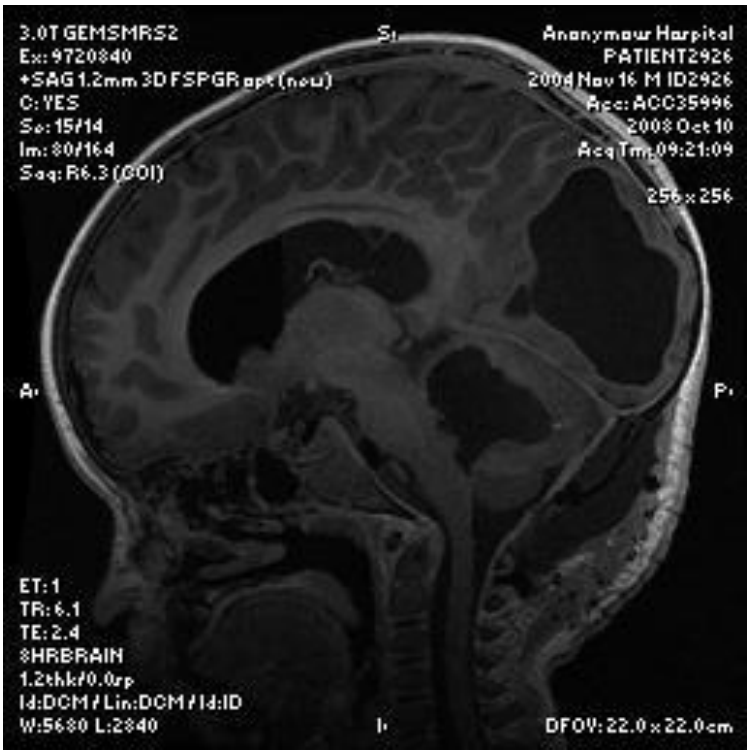
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Figure 5: Sheets of atypical cells in the solid choroid plexus carcinoma. (Hematoxylin & Eosin magnification X 200) *Inset*: Scattered atypical cells lining well-defined papillae of choroid plexus carcinoma. (Hematoxylin & Eosin magnification X 200)

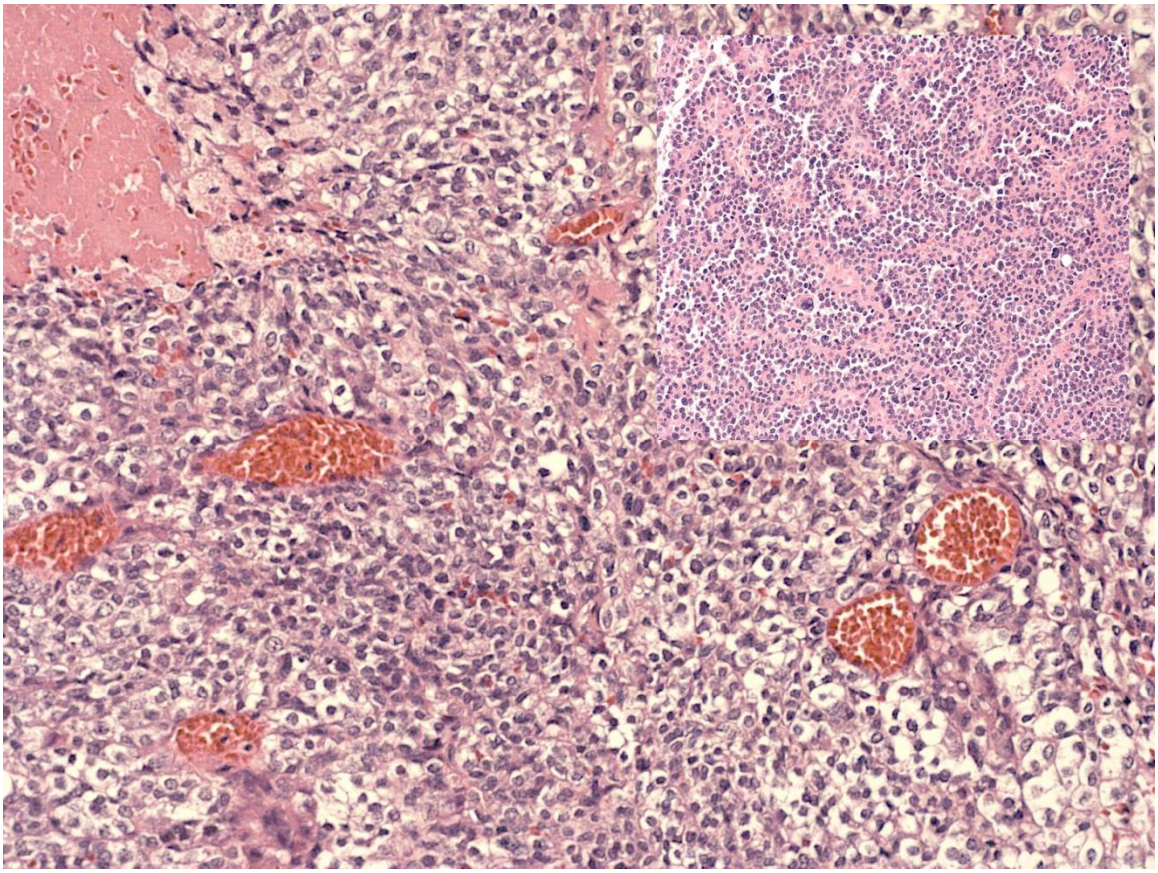
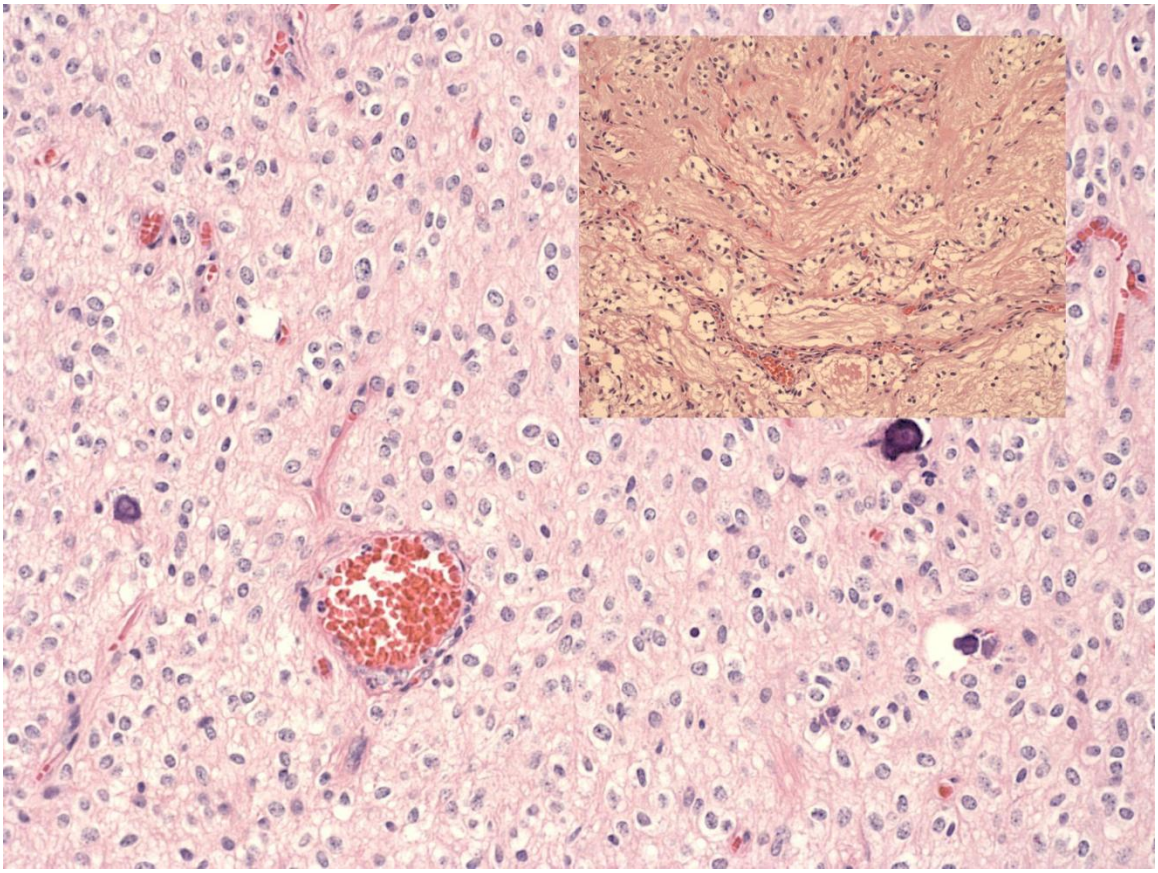


Figure 6: Oligodendroglial pattern with small cells with round uniform nuclei and perinuclear clearing, delicate capillaries and calcifications in low-grade astrocytoma (Hematoxylin & Eosin magnification X 100). *Inset*: Densely fibrillar "piloid" areas of low-grade astrocytoma involving the subarachnoid space. (Hematoxylin & Eosin magnification X 200)



Resolution of Chiari Malformation after Cerebellopontine Angle Arachnoid Cyst Fenestration A Case Report and Technical Review

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ABSTRACT

CPA arachnoid cyst are second only to middle fossa in terms of reported locations. Given this they are still rare entities which make up approximately 10% of all cases reported in the literature for arachnoid cysts These cysts may expand, compressing surrounding structures and produce neurological symptoms. The mass effect of the cyst effetely creates a smaller posterior cranial fossa volume there by displacing the cerebellum. This creates an "acquired" Chiari malformation. Indications for treatment are limited to those arachnoid cysts, which produce symptoms either through direct or indirect brain or cranial nerve compression. The goals of surgical intervention are to restore the communication between the cyst and subarachnoid space through fenestration, resection or shunting of the cyst

Objective: We present a case and review the literature of a patient who presented with a large CPA arachnoid cyst involving the cranial nerves V-XII producing mass effect on the cerebellum resulting in acquired Chiari 1 malformation.

Results: Given the patients symptomatology we elected to proceed with endoscopic cyst fenestration. At the end of the procedure the cerebellar tonsils had ascended above the foramen magnum and the cyst was fenestrated with the subarachnoid spaces of the prepontine cistern.

Conclusion: Endoscopic arachnoids cyst fenestration is a safe an effective means to treat both posterior fossa arachnoid cysts and acquired Chiari malformation

Key words: posterior fossa arachnoid cyst, endoscopic neurosurgery, acquired Chiari malformation

Introduction

Arachnoid cysts are congenital cerebrospinal fluid (CSF) collections located in the arachnoid membranes, subarachnoid space and cisterns (4, 7, 8, 11). Arachnoid cysts make up about 1 % of all intracranial mass lesions. They are most commonly located the middle cranial fossa and occur with greater frequency in children (5). Cerebellopontine Angle (CPA) arachnoid cysts are the second most common location (7, 11). CPA arachnoid cysts are usually located posterior and inferior to the cranial nerves VII/VIII complex (5). The developments of

arachnoid cysts are believed to result from the splitting or duplication of the arachnoid membrane, which alters CSF fluid dynamics from congenital, traumatic or infectious etiologies (10). Mass effects of posterior fossa arachnoid cysts have been documented to produce Chiari Type I malformation. Syringomyelia has been found to be related to the downward invagination of the cyst or the cerebellar tonsils into the foramen magnum (1, 8).

Clinical signs and symptoms of CPA arachnoid cysts develop from compression and dysfunction of neural structures due to mass effect. Most frequent symptoms result from increased intracranial pressure. Paroxysmal subocciptial headaches are a classic clinical presentation. Other symptoms include nausea, vomiting, ataxia, gait disturbance and cranial nerve dysfunction producing dyspahgia, nystagmus, hemi-facial spasm and facial nerve palsy (7, 11).

Indications for treatment of CPA arachnoid cysts include focal neurological deficit, intracranial hypertension and progressive non-localizing symptoms, (i.e. headache) (2, 6). The most common surgical treatment options include cyst-peritoneal shunting, craniotomy for microsurgical resection, marsupialization, and cyst fenestration as well as endoscopic approaches for cyst fenestration (2, 6).

Case Report:

The patient is a 49 y/o right handed female sent for consultation with a two-year history of headache on the top of her head after valsava maneuver. The patient complains of a six-month history of hearing loss and tinnitus in the left ear, and difficulty with balance. The patient also has mild complaints of numbness in the left V-3 distribution of the trigeminal nerve and occasional blepharospasm on the left. The patient denies vertigo or visual changes. The past medical and surgical history is otherwise unremarkable. On neurological examination: mentation, cranial nerve, strength, sensation examination are all grossly intact. There is mild difficulty with tandem gait on examination. Outpatient audiograms show moderate high frequency hearing loss on the left.

The MRI of the brain with and without gadolinium reveals large left cerebellar- pontine angle (CPA) hypointenstiy consistent with cerebrospinal fluid, consistent with an arachnoid cyst. There is also a Chiari malformation with extension of the cerebellar tonsils through the foramen magnum down to the lamina of C2. Cranial nerves V, VII, VIII, IX, X, and XI, all course through the cyst. (Figures 1-3).

The patient symptoms were attributed to the Chiari malformation, which was secondary to the mass effect of arachnoid cyst. The treatment options given to this patient included conservative management, endoscopic fenestration and marupilization of the cyst and Chiari decompression. The patient chose endoscopic fenestration with the understanding this may not resolve all of her symptoms, thus requiring a definitive Chiari decompression.

Operative Technique:

The patient underwent endotrachal intubation was then administered IV and inhalation anesthetic agents. The patient was then placed in a Mayfield head frame and the head was rotated to the right. A 2 cm left post- auricular skin incision was made. The dissection was carried to the bone. A 14 mm craniectomy was then made, after identifying the transverse- sigmoid sinus junction; a curvilinear incision was made in the dura. The endoscope was then introduced into the posterior fossa and CSF removed to decompress the CPA. The endoscope was then removed and a large arachnoid cyst was then opened and cranial nerves 3- 12 were then identified. (Figures) The dissection was carried down to the level of foramen magnum. The left cerebellar tonsil was then elevated into the posterior fossa. The ventral aspect of the cyst was then fenestrated to allow direct communication with the prepontine and interpeduncular cisterns. The endoscope was then with drawn and the dura was closed in the usual fashion. A cranioplasty was then performed; the skin was closed in the usual fashion.

Discussion

CPA arachnoid cysts have been described in the literature as early as 1957 by Nichols and Manganiello who described their patient with a large CPA arachnoid cyst with multiple cranial nerve and cerebellar symptoms mimicking the clinical presentation of an acoustic neuroma (7). CPA arachnoid cyst are second only to middle fossa in terms of reported locations. Given this they are still rare entities, which make up approximately 10% of all cases reported in the literature for arachnoid cysts (5, 7, and 10).

These cysts are typically the result of abnormal duplication of the arachnoidal membranes during brain development. The commonly accepted theory for the development of arachnoid cysts is believed to be from alterations of CSF flow through the primitive leptomeninges during the formation of the subarachnoid space producing a diverticulum which traps CSF in the and arachnoidal membrane. This alteration of CSF dynamics is theorized to be from infectious, traumatic or congenital etiology (5, 7, 10, and 11).

Development of Chiari 1 malformation with caudal displacement of the cerebellar tonsils below the foramen magnum and CPA arachnoid cysts has also been described in the literature(8). The cysts may enlarge through a ball-valve mechanism where fluid enters the cyst wall through an osmotic gradient and is retained in the cyst, there by enlarging it in size (10). The mass effect of the cyst effetely creates a smaller posterior cranial fossa volume there by displacing the cerebellum. This creates an “acquired” Chiari malformation. There is a pressure gradient, which is created by either increased intracranial pressure or hydrocephalus between the cranial and spinal compartments due to the mass effect of the CPA cyst (8, 10). Patients with Chiari 1 malformation present with symptoms related to compression neural structures at the foramen magnum.

Head and neck pain, cranial nerve dysfunction and cerebellar dysfunction are common clinical findings (8).

Asymptomatic arachnoid cysts should be managed expectantly. Indications for treatment are limited to those arachnoid cyst which produce symptoms either through direct or

indirect brain or cranial nerve compression. Other indications also include hydrocephalus, focal deficits or non-localizing symptoms which are progressive, i.e. headache. Incompetent communication between the cysts and subarachnoid space can produce either acute deterioration or slowly progressive symptoms (2, 6, 7). The goals of surgical intervention are to restore the communication between the cyst and subarachnoid space through fenestration, resection or shunting of the cyst (6).

Craniotomy allows direct visualization of the cyst wall and coagulation of the cyst membrane and arachnoidal blood vessels. The cyst is directly fenestrated into the subarachnoid space, without accumulitation of subarachnoid debris creating a possible obstruction of outflow and possible recurrence in the future (7). Potential complications of open surgery consist of aseptic meningitis, new on set of seizures and neurological deficit related to the procedure (2). Another treatment option is cyst- peritoneal shunting. A catheter is placed in the cyst and the distal terminal is placed in the abdomen. This is a less invasive, straightforward procedure and has shown to provide significant clinical benefit to patients with signs and symptoms consistent with intracranial hypertension. (2, 7) The major risks are associated with shunt malfunction/ revision and infection, and subdural hematoma (9).

Treating patients with "acquired" Chiari 1 malformation create a clinical dilemma. Patients with large CPA cysts with tonsillar descent and both cranial nerve and cerebellar dysfunction require treatment directed at the primary root cause of the pathology. Case reports have delineated the need to perform both a cyst fenestration or shunting and foramen magnum decompression(8, 10).

Endoscopic Surgery is a minimally invasive treatment option for posterior fossa arachnoid cysts. This modification of open surgery has been described by Schroder as early as 1996 . Gangemi in 2001 also reported two cases where large posterior fossa arachnoid cysts were treated through an endoscope. The introduction of the endoscope allows for direct inspection of the cavity and fenestration of the anterior wall into the subarachnoid space and prepontine cistern. CPA arachnoid cysts are best treated through a retro mastoid burr hole with fenestration of the cyst into then prepontine cistern between the trigeminal nerve and VII/VIII nerve complex . In order for endoscopic treatment to be possible requires open subarachnoid spaces around the cyst to enable endoscopic orientation for cyst fenestration (4, 9).

Conclusions

We present a case and review the literature of a patient who presented with a large CPA arachnoid cyst involving the cranial nerves V-XII producing mass effect on the cerebellum resulting in acquired Chiari 1 malformation. Given the patients symptomatology we elected to proceed with endoscopic cyst fenestration. At the end of the procedure the cerebellar tonsils had ascended above the foramen magnum and the cyst was fenestrated with the subarachnoid spaces

of the prepontine cistern. Follow up MRI showed resolution of the Chiari malformation and the arachnoid cyst.

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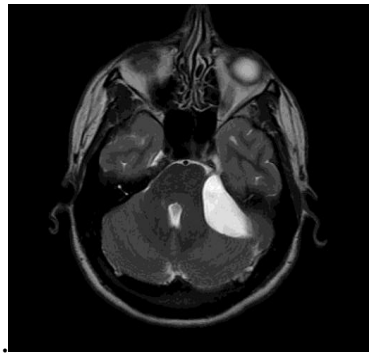
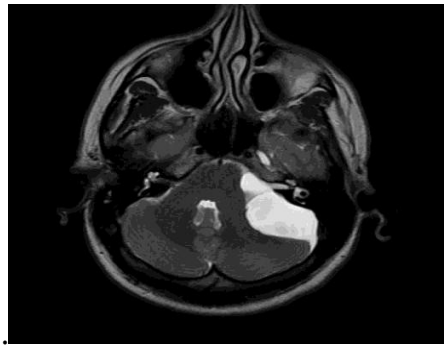
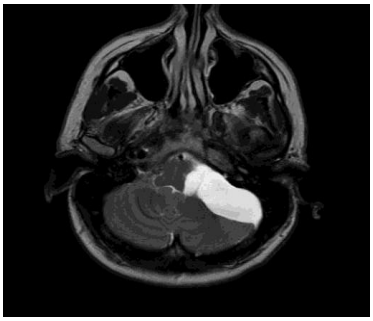
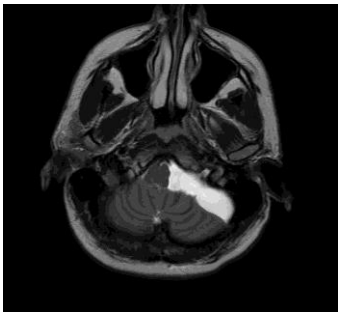
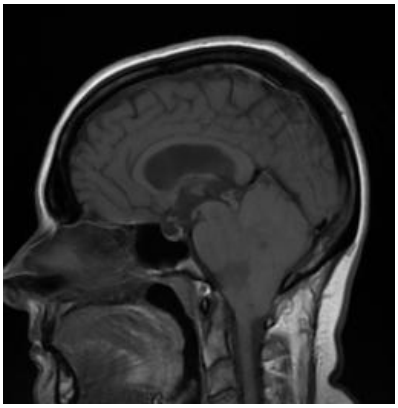
Figures

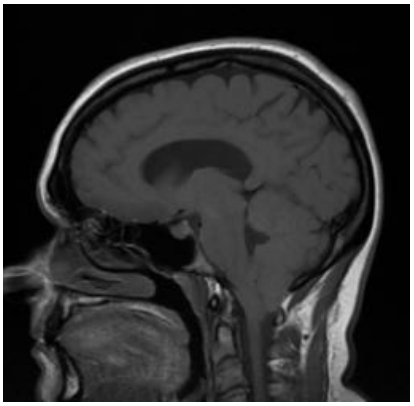
1. 

2. 

3. 

4. 

5. 

6. 

P1 to P1 Horizontal Enterprise™ Stent Deployment via The Posterior Communicating Artery for The Stent-Assisted Coiling of an Unruptured Wide-Neck Bilobed Basilar Tip Aneurysm

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Abstract

Stent-assisted coiling techniques have allowed for the embolization of challenging wide neck intracranial aneurysms. A technical description follows for the endovascular treatment of a wide-necked bilobed basilar terminus aneurysm with stent-assisted coil technique. A new Nitinol self expandable stent (Enterprise™, Cordis Endovascular, Miami Lakes, FL) was placed horizontally across the neck of the aneurysm through the right posterior communicating artery.

Key Words Aneurysm, Self-expandable stent, Stent assisted coiling

Introduction

Surgical treatment of basilar aneurysms holds the highest surgical morbidity and mortality among all aneurysms[1]. Basilar aneurysms are complicated to treat surgically given their deep location, rendering endovascular options more attractive [2] . Endovascular coil occlusion appears to be a safe and effective treatment for these selected unruptured intracranial aneurysms [3,4,5]. In more than 90% of embolization cases, near-complete aneurysm occlusion can be achieved[6]. Aneurysms with large neck-to-dome ratios, thrombosed aneurysms, and those with critical perforating arteries arising from the dome or neck still present a challenge for endovascular surgeons. Stent assisted coiling techniques have allowed for embolization of challenging wide neck intracranial aneurysms. Endovascular techniques for bifurcation aneurysms with large neck-to-dome rations include “kissing stents” [7], retrograde balloon-assisted remodeling technique [8], and the deployment of the neck-bridge device[9]. Previously described endovascular treatments for wide-necked basilar tip aneurysms involved deployment of a stent in a Y-configuration in the posterior cerebral arteries and the basilar artery [10,]. Additionally, a novel technique for the horizontal placement of a Neuroform stent (Target/BSC/Smart therapeutics, Fremont, CA) across the neck of a basilar tip aneurysm via the anterior circulation has been described previously. “Cross-over” technique via the contralateral internal carotid artery for horizontal stenting of an internal carotid bifurcation aneurysm has also been accomplished. In our case, the horizontal deployment of Enterprise ™ across the neck of a basilar tip aneurysm via the posterior communicating artery enabled safe coil delivery while preserving the parent vessels 11.

The Cordis Enterprise™ Vascular Reconstruction Device (VRD) is comprised of a self-expanding, Nitinol stent pre-loaded in a delivery wire. This stent is intended for use with embolic coils for the treatment of wide-neck, intracranial, saccular, or fusiform aneurysms arising from a parent vessel with a diameter of ³ 3 mm and £ 4 mm. The stent has a closed-cell structure, which measures 4.5 mm x 22 mm. Radiopaque tantalum markers are present on 4 struts at either end of the device for in vivo visualization. The device is recapturable up to two times.

CASE REPORT

The patient is a 56-year-old, white female with multiple medical problems including SLE, constrictive pericarditis, mitral valve prolapse, hyperlipidemia, hypertension, and generalized anxiety disorder, which was seen by her primary care physician for cephalgia. The patient was found to have an incidental aneurysm of the basilar tip on MR and subsequent angiography (Fig A).

Intervention

Institutional review board approval was obtained. The patient signed consent for the use of the Enterprise™ stent, which is a humanitarian use device. The patient had been premedicated with aspirin 325mg and Plavix 75mg (Bristol-Myers Squibb/Sanofi Pharmaceuticals, New York, NY) for planned stent placement. The patient was placed under general anesthesia and heparinized. Shealths were placed into bilateral femoral arteries (Cordis Endovascular, Miami Lakes, FL). Intracranial cerebral angiography was performed which revealed 7-8 mm x 4-5 mm bilobed basilar tip aneurysm with a wide neck, unchanged from prior angiography. A larger 5 mm lobe projected anteriorly with a 4 mm lobe projecting posteriorly (Fig. 5, 1.13.12).

First, a 6-French guide catheter was then used to select the right common carotid artery for cervical angiography. This showed normal filling of the anterior and middle cerebral artery and large right posterior communicating artery with flash filling of the basilar tip region (Fig 10). The guiding catheter was then left on a continuous heparinized flush system. Next, a 5-French

Envoy guide catheter was used to select the right vertebral artery through the left femoral sheath. This was done with standard wires and angiography. A Prowler Select Plus microcatheter (2.8-French; Cordis Endovascular, Miami Lakes, FL) was then used with a Synchro 14 wire (Target/BSC) to select the posterior communicating artery. Roadmapping on the lateral view was done for the internal carotid artery and roadmapping on the AP view was done from the right vertebral artery injection.

The microcatheter and wire were then used to easily traverse the posterior communicating artery from the internal carotid artery into the P1 segment of the right posterior cerebral artery. The catheter was advanced across the neck of the aneurysm at the basilar tip and into the left P1 segment terminating in the P2 segment. This microcatheter was then placed on a

continuous heparinized flush system. Next, a pre-shaped Prowler 14 microcatheter (Cordis Endovascular, Miami Lakes, FL) was used through the vertebral guidecatheter to select the basilar artery. A roadmap technique was used to place the microcatheter into the anterior lobe of the aneurysm, making sure to stay ventral to the previously placed guiding catheter horizontally placed across the neck of the aneurysm. Once positions were confirmed, an Enterprise stent (Cordis Endovascular, Miami Lakes, FL) was advanced via a carotid guiding catheter across the neck of the aneurysm from P1 to P1 segment. It was positioned across the neck of the aneurysm and angiography was performed to confirm its position (Fig B). The stent was deployed uneventfully from the P1 to the P1 segment. Angiography after stent deployment showed complete expansion of the stent, with a microcatheter jailed into the anterior lobe of the aneurysm (Fig C). Once this was confirmed, the microcatheter that had delivered the stent was removed from the internal carotid artery completely.

Coiling was then initiated through the microcatheter, which was jailed by the stent in the anterior lobe of the aneurysm (Fig D). First, a GDC 360, 5 x 15 (Target/BSC) was used to frame the anterior and mid portion of the aneurysm. Angiography confirmed that the coil was abutting the stent prior to detachment. Next, a 4 x 8 Cerecyte bioactive coil - Helipaq 10 (Micrus Endovascular, San Jose, California) was placed, followed by a 3 x 6. Angiography demonstrated patency of the stent and parent vessels, therefore the coils were detached. A Synchro 14 wire (Target/BSC) was then used with an Echelon 10 (MTI, Irvine, Calif) which allowed selection of the posterior lobe of the aneurysm. This was coiled with a Helipaq 10, 3 x 6 coil (Micrus Endovascular, San Jose, California) which framed the posterior lobe of the aneurysm. Another coil 2 x 4 was attempted, but the microcatheter pushed out into the stent and it was therefore removed and this coil was not placed. The microcatheter was then removed without difficulty.

Final angiography demonstrated complete occlusion of the anterior aspect of the aneurysm and mid aspect with trace filling into the posterior aspect, with slightly loose packing posteriorly. The stent remained widely patent as did bilateral posterior cerebral arteries. There were no distal thromboembolic complications appreciated. The catheters were all removed, and closure devices were utilized to maintain hemostasis in bilateral femoral arteries. The patient awoke without neurological sequelae.

Discussion

The goal for the endovascular treatment of basilar tip aneurysms is complete coil obliteration, given the high risk of aneurismal recurrence [6]. Terminal wide-neck aneurysms of the basilar artery present a unique challenge in accomplishing this goal. The placement of a stent perpendicular to the neck of the aneurysm may prevent coil relapse [11]. Previously described techniques involved deployment of stents in a Y-configuration in the posterior cerebral arteries and the basilar artery [7]. Unfortunately, this procedure utilizes multiple stents which may increase the risk of thomboembolic complications. Additionally, access to the neck of the

aneurysm for coiling may be limited given the Y shaped position of the stents at the origin of the aneurysm.

The posterior communicating artery approach to basilar terminus aneurysms has been described previously [11]. The successful performance of such an approach requires the presence of a sizable posterior communicating artery. Additionally, both P1 segments must be patent and of similar girth to allow to complete expansion of the stent. When performed correctly, this technique may allow for better approximation to the neck of the aneurysm [11]. Cross, et al. states stent placement may potentially divert blood flow away from the coil mass within the aneurysm sac, theoretically preventing recurrence and therefore recurrent rupture of the aneurysm. Additionally, thromboembolic complications may be decreased when compared to endovascular techniques which require the use of multiple intracranial stents[7,11]. When compared to procedures which utilize two stents, the placement of a single horizontal stent across the base of an aneurysm is cost-effective.

In our case, new Nitinol self expandable stent (Enterprise™, Cordis Endovascular, Miami Lakes, FL) was utilized to accomplish horizontal stenting across the base of a basilar tip aneurysm. The Enterprise™ stent has a closed cell design, and can be used without additional balloons. This reduces the risk of intimal arterial injury and subsequent thromboembolic complications. In our experience, the Enterprise™ stent outperforms the other intracranial stents in regards to ease of tractability and flawless deployment. In our case, navigation of the Circle of Willis was accomplished effortlessly. Deployment of the stent from P1 to P1, across the basilar tip was uneventful. The coils properly conformed to the surface of the stent, allowing for aneurismal coil occlusion. No clinical neurological sequelae resulted.

Also reported in our case was the use of two femoral shealths, allowing for the placement of dual intracranial microcatheters. One microcatheter was placed into the anterior lobe of the aneurysm, and a second microcatheter was placed via the anterior circulation for stent placement. The microcatheter placed into the anterior lobe of the aneurysm was thus pinned by the stent after deployment (Fig). The potential difficulties associated with placing a microcatheter through two walls of the stent was avoided.

Conclusion

In conclusion, horizontal stenting techniques have expanded the armamentarium of the endovascular surgeon. This unique approach of accomplishing stent assisted coil embolization of wide-necked and bifurcation intracranial aneurysm remains an appealing option for certain patients. The successful performance of such an approach requires the presence of a sizable posterior communicating artery and patent P1 segments bilaterally.

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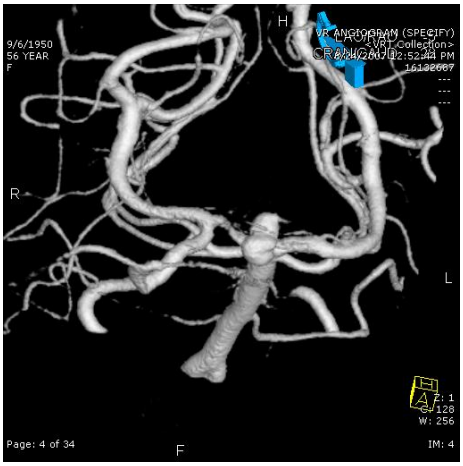

Fig. A 3D angiogram image demonstrating a bilobed wide neck basilar tip aneurysm.

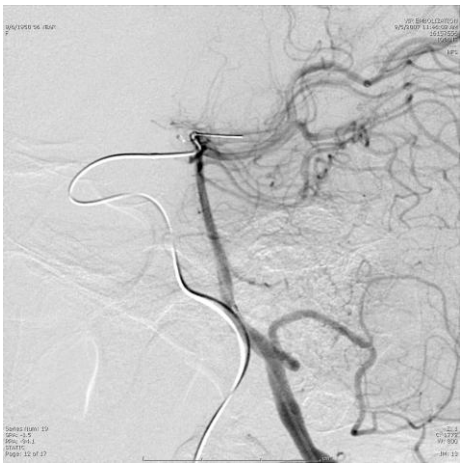
Fig B Microcatheter seen in the anterior circulation tracking through the PCOM and into the contralateral PCA.

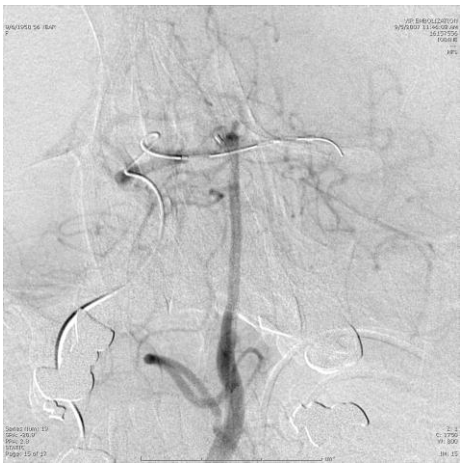
Fig C. Demonstrating two microcatheters in place. The first is seen crossing from the anterior circulation across bilateral PCAs prior to stent deployment. The second is seen in the posterior circulation with distal tip in the basilar aneurysm.

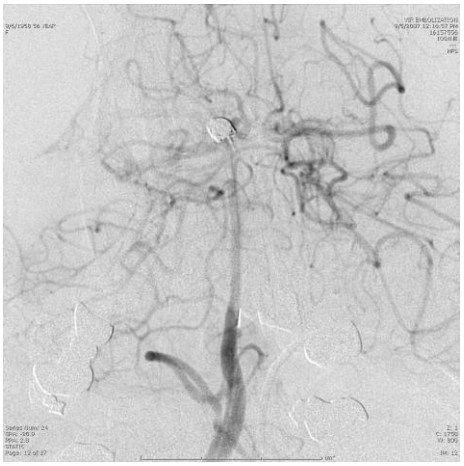

Fig D. Stent has been released in this image and GDC has initiated. The microcatheter is seen passing through the stent.